AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1-46. (Cancelled).

47. (Currently Amended) Library comprising a plurality of tagged ligands of formula I

$$(Lig\ J_L)_m \quad L\ (J_T\ Tag)_m(J_T\ L\ (J_L\ Lig)_m)_p$$

and salts thereof wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers

comprising one or a plurality of same or different ligand moieties Lig each linked to one or a plurality of same or different tag moieties Tag via same or different linker moieties L and same or different linking site or linking functionality J_T and J_L

wherein Lig is a ligand selected from a non-peptide ~~comprises a~~ GPCR ligand agonist and a non-peptide GPCR ligand antagonist, wherein the Lig comprises pharmacological activity as an agonist or antagonist for GPCR receptor binding and activation or inhibition, ~~an inhibitor of an intracellular enzyme or a substrate or inhibitor of a drug transporter~~

L is selected from ~~a single or double bond~~ , ~~-O-~~, ~~-S-~~, amine, ~~COO-~~, amide, ~~-NN-hydrazine; and~~ saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}600}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P,

wherein optional substituents are selected from any C_{1-20} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano and carbonyl and combinations thereof, and L ~~may be~~ is monomeric, oligomeric having oligomeric repeat of 2 to 30 or polymeric having polymeric repeat in excess of 30 up to 300;

Tag is any tagging substrate;

m are each independently selected from a whole number integer from 1 to 3;

p is 0 to 3

wherein one or more of each -Tag in one or more or each library compound is a fluorophore entity -Fl, whereby the library comprises compounds of which one or more or all of which are of formula I'

$(LigJ_L)_m$ L $(J_T\ Fl)_m(J_TL(J_LLig)_m)_p$

characterised in that linking is at same or different linking sites in compounds comprising different Lig, J_L, L J_T and/or – Tag and is at different linking sites in compounds comprising same Lig, J_L, L J_T and/or – Tag

wherein the or each Fl is selected from a red, near ir or blue dye,

and the compound of formula I or I' retains pharmacological activity as a fluorescent GPCR ligand agonist or fluorescent GPCR ligand antagonist or GPCR receptor binding and activation or inhibition.

48. (Withdrawn and currently amended) Library comprising a plurality of tagged ligands of formula I

$$(Lig\ J_L)_m\ L(J_T Tag)_m(J_T L(J_L Lig)_m)_p$$

and salts thereof wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers

comprising one or a plurality of same or different ligand moieties Lig each linked to one or a plurality of same or different tag moieties Tag via same or different linker moieties L and same or different linking site or linking functionality J_T and J_L

wherein Lig ~~comprises a GPCR ligand, an inhibitor of an intracellular enzyme or a substrate or inhibitor of a drug transporter;~~ is a ligand selected from a non-peptide GPCR ligand agonist and a non-peptide GPCR ligand antagonist, wherein the Lig comprises pharmacological activity as an agonist or antagonist ~~of~~for GPCR receptor binding and activation or inhibition,

L is selected from ~~a single or double bond, O , S ,~~ amine, ~~COO ,~~ amide, ~~NN hydrazine; and~~ saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}600}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, wherein optional substituents are selected from any $C_{1\text{-}20}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano and carbonyl and combinations thereof, and L ~~may be~~ is monomeric, oligomeric having oligomeric repeat of 2 to 30 or polymeric having polymeric repeat in excess of 30 up to 300;

Tag is any tagging substrate;

m are each independently selected from a whole number integer from 1 to 3;

p is 0 to 3

wherein one or more of each -Tag in one or more or each library compound is a fluorophore entity -Fl, whereby the library comprises compounds of which one or more or all of which are of formula I'

$(LigJ_L)_m$ $L(J_T\ Fl)_m(J_TL(J_LLig)_m)_p$

characterised in that linking is at same or different linking sites in compounds comprising different Lig, J_L, L J_T and/or – Tag and is at different linking sites in compounds comprising same Lig, J_L, L J_T and/or – Tag,

wherein the or each Fl is selected from the following dyes: Texas red™, coumarin and derivatives, Cascade Blue™, EvoBlue and fluorescent derivatives thereof, pyrenes and pyridyloxazole derivatives, the cyanine dyes, the dyomics (DY dyes and ATTO dyes) and fluorescent derivatives thereof, the Alexafluor dyes and derivatives, BDI dyes including the commercially available Bodipy™ dyes, pyrenes, anthracenes, acridines, fluorescent phycobiliproteins and their conjugates and fluoresceinated microbeads, and Texas Red derivatives, coupled to amine groups using the isocyanate, succinimidyl ester or dichlorotriazinyl-reactive groups,

and the compound of formula I or I' retains pharmacological activity as a fluorescent GPCR ligand agonist or fluorescent GPCR ligand antagonist or GPCR receptor binding and activation or inhibition.

49. (Withdrawn-Previously Presented) Library as claimed in Claim 47 wherein each compound of formula I or I' comprises one of a plurality of fluorophores and/or tags providing a library of differently fluorescently tagged ligands comprising one or a number of different fluorophores optionally of different chemical composition or spectral characteristics; and/or providing a library of differently tagged ligands including at least one fluorescently tagged ligand; alternatively each compound of formula I or I' comprises one of a plurality of precursor ligands linked each to one or a plurality of different tags providing a library of same or differently tagged ligands of plural ligand type; alternatively each compound of formula I comprises one of a plurality of linkers linking a precursor ligand and at least one Tag at the same or different linking site; alternatively each compound of formula I or I' comprises the same linker linking a precursor ligand and at least one Tag at different linking sites providing a library of differently linked tagged ligands of different conformation or anticipated pharmacology and binding.

50. (Withdrawn) Library as claimed in Claim 47 comprising a plurality of compounds of one or more of formula II to III:

II $(LigJ_L)_m$ L J_T TagJ_T L $(J_L$ Lig$)_m$ where each m is as hereinbefore defined and is preferably 1 or 2, more preferably 1

III $(LigJ_L)_m$ L $(J_T$Tag$)_m$ wherein each m is as hereinbefore defined and is preferably 1 and/or 2, more preferably

Lig J_L – L – J_L Tag and/or

Lig J_L – L – J_T Tag and/or Lig J_L – L – J_T Tag

$\diagdown J_L$ Lig $\diagdown J_T$ Tag

wherein each J_L and J_T comprises J as hereinbefore defined and may be same or different and may derive from functionality originally present in Lig or L and Tag or L or a combination thereof, characterised in that linking is at same or different linking sites in compounds comprising different Lig, J_L, L, J_T and/or Tag, and is at different linking sites in the case of any two or more compounds comprising identical Lig, J_L, L, J_T and/or Tag.

51. (Withdrawn-Currently Amended) Library as claimed in Claim 47 ~~including information for~~ wherein each compound of formula I ~~comprised in the Library, relating to the~~ has verified pharmacology for binding to or inhibition of a GPCR receptor ~~or to inhibition of an intracellular cyclic nucleotide phosphodiesterase, or inhibition of or transport by a drug transporter~~ including designation as agonist or, antagonist~~, substrate or inhibitor~~ and measure of affinity or inhibition, enabling quantification of results.

52. (Withdrawn-Currently Amended) Library as claimed in Claim 47 wherein ~~a GPCR ligand~~ Lig is selected from any compound which is effective as an agonist or antagonist for an adenosine receptor, a beta-adrenoceptor, a muscarinic receptor, a histamine receptor, an opiate receptor, a cannabinoid receptor, a chemokine receptor, an alpha-adrenoceptor, a GABA receptor, a prostanoid receptor, a 5-HT (serotonin) receptor, an excitatory aminoacid receptor (glutamate), a dopamine receptor, a protease-activating receptor, a neurokinin receptor, an angiotensin receptor, an oxytocin receptor, a leukotriene receptor, a nucleotide receptor (purines and pyrimidines), a calcium-sensing receptor, a thyroid-stimulating hormone receptor, a

neurotensin receptor, a vasopressin receptor, an olfactory receptor, a nucleobase receptor (adenosine), a lysophosphatidic acid receptor, a sphingolipid receptor, a tyramine receptor (trace amines), a free-fatty acid receptor and a cyclic nucleotide receptor; ~~an inhibitor of intracellular enzymes is an inhibitor of cyclic nucleotide phosphodiesterases; and a substrate or inhibitor of a drug transporter is selected from a substrate or inhibitor of an equilibrium based drug transporter or ATP driven pump selected from a catecholamine transporter, a nucleoside transporter, an ATP-binding cassette transporter, a cyclic nucleotide transporter or derivatives or analogues thereof ;~~

or wherein Lig is selected from

a) xanthine like structures including XAC, theophylline, caffeine, theobromine, dyphilline, enprofylline; or fused biaryl structures including papaverine, dihydroquinilones, cilostamide, dipyridamole or vinpocetine; and analogues thereof;

b) adenosine like structures including ADAC, NECA and analogues thereof;

c) ethanolamine like structures including salmeterol, salbutamol, terbutaline, quinprenaline, labetalol, sotalol, bambuterol, fenoterol, reprotolol, tulobuterol, clenbuterol and analogues thereof;

d) oxypropanolamine like structures including CGP12177, propranolol, practolol, acebutalol, betaxolol, ICI 118551, alprenolol, celiprolol (celectol), metoprolol (betaloc), CGP20712A, atenolol, bisoprolol, misaprolol, carvedilol, bucindolol, esmolol, nadolol, nebivolol, oxprenolol, xamoterol, pindolol, timolol and analogues thereof;

e) xanthine like structures including XAC, theophylline, caffeine, theobromine, dyphilline, enprofylline, sildenafil, EHNA (erythro-9-(2-hydroxyl-3-nonyl)adenine), zaprinast; or spiro

bicyclic structures including bypyridines, amrinone; imidazolines, CI930; dihydropyridazinones, indolan, rolipram, SB207499; or fused biaryl structures including papaverine, dihydroquinilones, cilostamide, dipyridamole, vinpocetine and analogues thereof.

53. (Withdrawn) Library as claimed in Claim 47 wherein J_{Lm} L J_{Tm} comprises a mono, di, tri, tetra, penta, or hexa amino, alkylthio, alkoxy, carboxylic acid, and combinations thereof including a mono, di or tri aminoalkylthio, amino alkoxy, alkoxy carboxylic acid or alkoxy amine, mono, di or tri amino menthane, amino ethane, thio ethane, ethane, amino acyl, polypeptide, or mono or polyether derivatives including diamine or dithio derivatives, mono or polyethylene glycol di or tri amine or thio;

or comprises a mono-, di-, tri- or tetra, penta or hexafunctional linear or branched or cyclic substituted or unsubstituted hydrocarbyl of formula –L.I-

$J [A] q_L R_L [A'q_{L'} J']_p A''q_{L''} J''$

wherein each of J to J'' is a linking site or functionality as hereinbefore defined independently selected from a single or double bond, methylene, alkyne, alkene, NR, O, CONR, NRCO, S, CO, NCO, CHHal and P wherein R is H or C_{1-8} alkyl or cycloalkyl or forms part of a cyclic ring with N, Hal is any halogen selected from chlorine, iodine, bromine; and is present in any rational location in a group A to A'';

each of A to A '' is a group selected from –O-, -C(=O)-, C_{1-12} alkoxy, alkoyl, cycloalkyl, heterocyclic, alkyl, alkenyl, aryl, arylamide, arylamine, amino, thioalkyl, heteroaryl as

hereinbefore defined and combinations thereof, optionally substituted by groups selected independently from C_{1-3} alkyl and C_{1-5} alkoxy;

each of q_L to q_L'' are independently-selected from 0 or 1 or indicates an oligomeric repeat and is from 2 to 30, or indicates a polymeric repeat unit and is from 31 up to 300.

R_L is a C, N or S atom or is a $CR_{L'}$, $NR_{L'}$, alkyl, cycloalkyl, heterocyclic, aryl heteroaryl, amine or thio moiety and provides for branching when p is 1 or 2; wherein $R_{L'}$ is H or C_{1-3} alkyl; and

p is as hereinbefore defined and is 0, 1 or 2.

54. (Withdrawn) Library as claimed in Claim 47 wherein J_{Lm} L J_{Tm} is of formula

J Aq_L R_L J''

wherein each of J and J'' is amine or –O-, A is CH_2CH_2O, q_L is 1-30 or 31 to 300 and R_L is

CH_2CH_2

or of formula

J Aq_L R_L(A'J') J''

wherein each of J, J' and J'' independently is amine, –O or a single bond, q_L is 1, 2 or 3 -30 or 31 to 300 and A is CH_2CH_2O or $HNCH_2CO$ or q_L is 1 and A is C(O) or $(CH_2)_{1-8}$ or q_L is 0, R_L is CH or CH_2CH, $q_{L'}$ is 0 or q_L' is 1 and A' is CH_2 and $q_{L''}$ is 0

preferably

$O(CH_2CH_2O)q_LCH_2CH_2NH$, $O(CH_2CH_2O)q_LCH_2CH(CH_2NH)NH$,

$OCH(CH_2NH)NH$, -$CH(CH_2NH)NH$, -C(O) NH-, -$(CH_2)_{1-8}$- or (-$HNCH_2CO$-)$_{1-3}$ (= -gly_{1-3}-) -.

55. (Withdrawn and Currently Amended) Library as claimed in Claim 47 wherein each compound of formula I or I' comprises a moiety Lig and L as hereinbelow defined:

Wherein:

any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers

Lig.a_m is suitably of the formula, in either of the following forms given, including any of its possible linking configurations or sites:

Lig.$a^1{}_m$

Wherein at least one or all of Ra^1 to Ra^4, X^1 and X^2 comprise a linking site or functionality J as hereinbefore defined

X^1 and X^2 are each independently selected from H, O, OR.a, NR.a, NHR.a;

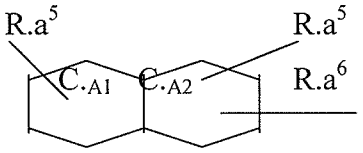
X^1 and X^2 are each preferably O;

each of $R.a^1$, $R.a^2$, $R.a^3$ and $R.a^4$ independently is selected from H or C_{1-4} linear or branched alkyl optionally mono or multi hydroxy or halo substituted;

$R.a^4$ is selected from a heteroatom O, S or substituted or unsubstituted amine or saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo and cyano; including optionally substituted aryl, cycloalkyl, alkyl, ketone, (di)amine, (di)amide, alkoxy, cycloalkyl, carboxylic

acid or optionally o-, m- or p- substituted phenyl wherein substituents include aryl, alkyl, cycloalkyl, heteroaryl or heteroalkyl, amine, amide, carboxyl, carbonyl or R.a^4 comprises cyclohexyl, cyclopentyl, ethoxy, $(CH_2)_2PhPh$, CH_2Ph, $CONH(CH_2)nCONH$, $CH_2CONH(CH_2)_2NH$, $CH_2PhNHCOCH_2$, $CH_2CH_2OCOCH_2$, succinimidyl ester, $NHCOCH_2$, $CH_2(CH_3)NCOCH_2$, $H_2N(CH_2)_2NHCOCH_2$, $H_2N(CH_2)_8NHCOCH_2$, $H_2NNHCOCH_2$, $CH_2CONH(CH_2)_2NHCOCH_2$, $HOPhCH_2N(CH_2CH_3.HOAc)(CH_2)_2NHCOCH_2$, heterocyclic-$(CH_2)_4CONH(CH_2)_2NHCOCH_2$ or heterocyclic-NHCON(heterocyclic)$COCH_2$;

or Lig.a is of the formula Lig.a^2-

Lig.a^2 

wherein at least one or all of Ra^5 to Ra^6, or a cyclic C or heteroatom comprise a linking site or functionality J as hereinbefore defined, each of $C._{A1}$ and $C._{A2}$ is independently selected from C_{5-6} aryl, heteroaryl, cycloalkyl and heterocyclic, more preferably from phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring –C=C- group; Each of up to seven R.a^5 is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from H, halo, hydroxy, thiol, amine, COOH, hydrazine, cyano, saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo =O or cyano; OCH_3, $CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

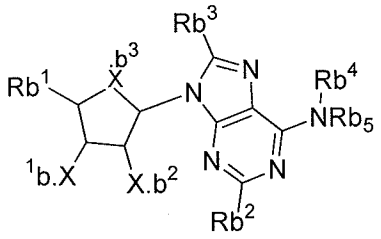
or any two or more of R.a^5 form a one, two or three ring fused cyclic structure, a fused 3 ring aryl, 5-heterocyclic or 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic Lig.a^{2}structure;

and $R.a^6$ is a moiety as defined for $R.a^5$ above;

and L.a is as hereinbefore defined for L or J_L L J_T or L.I or subformulae as hereinbefore defined, or is ~~a single bond,~~ amino acid or amide including a peptide or polypeptide gly or gly_3, alkyl of formula $-(CH_2)_n$ where n is 3 to 8, optionally including one or more heteroatoms or unsaturated groups, including –O- or –S- or –CH=CH-:

Lig.b is suitably of the formula Lig.b including any of its possible linking configurations or sites:

Lig.b



wherein at least one or all of Rb^1 to Rb^5 or Xb^1 to Xb^3 comprise a linking site or functionality J as hereinbefore defined

ring substituents $X.b^1$ and $X.b^2$ are independently selected from hydrocarbon including alkyl or SR_X, $NR_{X.2}$ and OR_X wherein (each) R_X is selected from H, $C_{1\text{-}5}$alkyl, alkenyl;

ring heteroatom $X.b^3$ is selected from –S-, -O- and $-CH_2$-;

Rb^1 is selected from saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}4}$ aliphatic, or $C_{1\text{-}3}$ alicyclic optionally including one or more heteroatoms N, O, S, P, wherein substituent(s) are selected from one or more cycloalkyl, heterocyclic, hydroxy, oxo, halo, amine; or $R.b^1$ comprises a carbonyl substituted by H, alkyl or a linear or cyclic primary, secondary or tertiary amine, substituted $C_{1\text{-}3}$ alkyl, cycloalkyl or amide, cyclopropyl, or $CONHC_{1\text{-}3}$alkyl including CONHEt or CH_2OH

and each of $R.b^2$ and $R.b^3$ is selected from H, halo, hydroxy, thiol, amine, COOH, CHO, hydrazine, cyano or saturated or unsaturated, substituted or unsubstituted

C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano, preferably from H, halo or hydroxy;

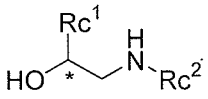
Rb^4 is H;

Rb^5 is H or alkyl

L.b comprises a linking site or functionality J as hereinbefore defined; and is as hereinbefore defined for L or its subformulae, more preferably is saturated and unsaturated substituted or unsubstituted C_{1-12} aliphatic or C_{1-24} aromatic as defined for L optionally including one or more heteroatoms O, S or N, cyclic or heterocyclic groups, or is of formula L.I or its subformulae as hereinbefore defined, or is (CH_2)m wherein m is 2 to 12, or is $(Ph\text{-}CH_2CONH)_2$ $(CH_2)_2$;

Lig.c is of the formula Lig.c including any of its possible linking configurations or sites:

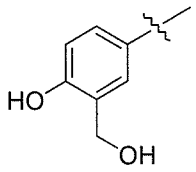
Lig.c $HOC^*(R.c^1)CH_2NH\text{-}R.c^2$



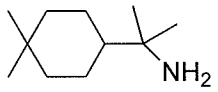
where at least one or all of Rc^1 to Rc^2 or OH, or a chain C or N comprise a linking site or functionality J as hereinbefore defined

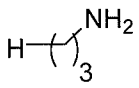
* indicates an optically active centre and

wherein $R.c^1$ is C_{6-14} aryl optionally including one or more heteroatoms selected from H, O, optionally substituted by OH, Hal, NH_2, NHC_{1-3}alkyl, sulphonamide, oxoamine or $(\text{-}CONH_2)$, or is mono, di or tri substituted phenyl or quinoline wherein substituents include OH, Cl or NH_2, or is m-CH_2OH, p-OH phenyl, m-,p-dihydroxy phenol or m-,m-dihydroxyphenol, m-,m-diCl, p-NH_2 phenol, p-OH, m-$CONH_2$ phenol or 5-OH, 8-quinoline,



R.c^2 is selected from saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any optionally substituted C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano and combinations thereof; or R.c^2 is selected from C_{1-6} branched or straight chain aliphatic, C_{6-10} araliphatic optionally substituted by OH and optionally including heteroatoms selected from N,O, optionally including an ether O, and is selected from $-(CH_2)$-$_6OCH((CH_2)_3Ph)$, $CHCH_3(CH_2)_2Ph$, $CHCH_3CH_2PhOH$, $C(CH_3)_2CH_2Ph$ or from the structures:

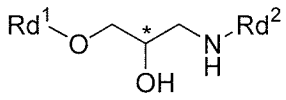




L.c is present as R.c^2 or comprises a linking site or functionality J as hereinbefore defined, and is as hereinbefore defined for L, formula L.I or its subformulae as hereinbefore defined, or is selected from C_{1-12} alkyl, amide;

Lig.d is of the formula Lig.d including any of its possible linking configurations or sites:

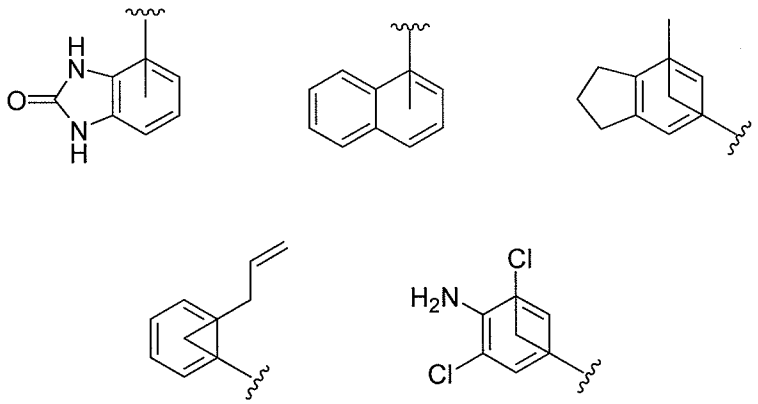
Lig.d $R.d^1\ OCH_2C^*HOHCH_2NH\text{-}R.d^2$



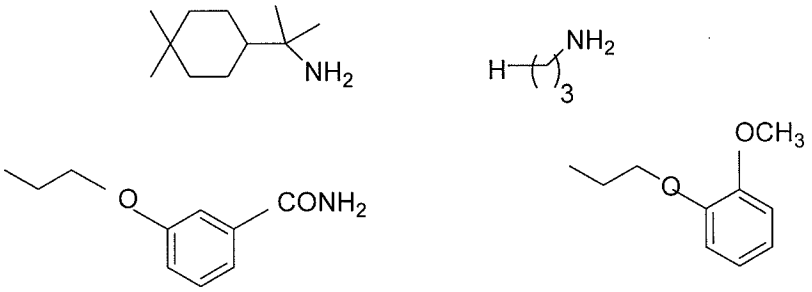
where at least one or all of Rd^1 to Rd^2 or OH, a chain C or N comprise a linking site or functionality J as hereinbefore defined

* indicates an optically active centre

wherein $R.d^1$ is saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano; or $R.d^1$ is substituted or unsubstituted C_{1-24} aralkyl or heteroaralkyl, including single ring and fused ring systems with (hetero)aryl or cycloalkyl rings, wherein optional substituents include C_{1-6} alkyl, alkoxy, ether, carbonyl, alkenyl, amine, amide each optionally carbonyl, amide, halo or OH substituted, or halo or OH, amine, amide, carbonyl, ketone, ether substituted phenyl or naphthyl, mono-, di-, tri- or tetra substituted mono or polycyclic fused aryl or cycloaryl or heterocycloaryl including phenyl, carbazole or structures shown below or spiro ring systems, mono-, di-, tri- or tetra alkoxyalkyl, alkoxyalkoxyalkyl or CF_3 substituted phenyl or unsubstituted or monosubstituted naphthalene or 5,6 ring systems:



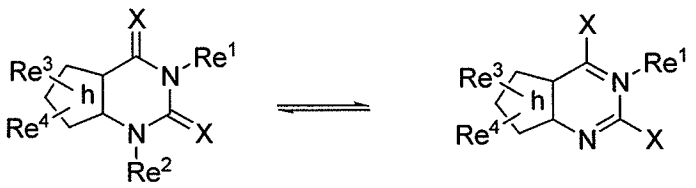
R.d^2 is substituted or unsubstituted amine, saturated or unsaturated, substituted or unsubstituted C_{1-12} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano, more preferably amine, C_{1-6} branched or straight chain alkyl optionally including ether O, and optionally substituted by C_{6-10} aryl, or of the formula:



L.d may be present as R.d^2 or may comprise a linking site or functionality J as hereinbefore defined and is as hereinbefore defined for L and its subformulae , formula L.I and its subformulae as hereinbefore defined, ~~or is a single bond~~ or is as hereinbefore defined for L.a;

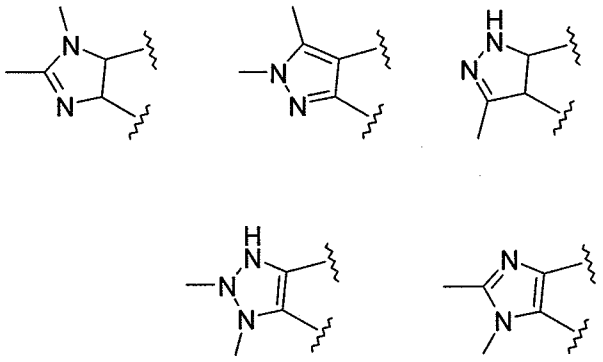
Lig.e comprises a cell permeant moiety or is associated with a cell permeant L or Fl moiety or is of the formula , in either of the following forms given including any of its possible linking configurations or sites:

Lig.e[1]



wherein at least one or all of Re^1 to Re^4, X and a ring C or N comprise a linking site or functionality J as hereinbefore defined

h is selected from



each optionally substituted by $R.e^3$ – $R.e^4$ wherein $R.e^1$ – $R.e^4$ are as $R.a^1$ – $R.a^4$ defined above or in which $R.e^3$ is C_{5-9} linear or branched alkyl, optionally mono or multi hydroxy or halo substituted or is aryl optionally substituted by alkoxy or sulfonyl,

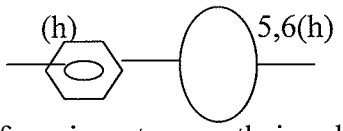
ortho-OEt, meta-SO_2N  NCH_3

each X is independently selected from H, O, -$OR.e^2$, N, HN, $NR.e^5$, $HR.e^6$, and aryl optionally substituted by ether; or X is aryl optionally alkyl or alkoxy substituted or is Ph-ortho-$OCH_2CH_2CH_3$;

and where R.e^5 is as defined above for R.e^1 above or forms a fused cyclic ring together with the adjacent ring N atom, or 1 or 2 fused 5 membered cyclic rings;

and R.e^6 is as defined above for R.e^1 above or is selected from optionally substituted phenyl wherein optional substituents include ether, o-ethoxy or o-propoxy, alkyl or OH, sulphonyl or carbonyl substituted by heterocyclic, or cyclic C_{5-8} alkyl, piperazinyl or sulphonyl;

or Lig.e is of the formula Lig.e^2

Lig.e^2 

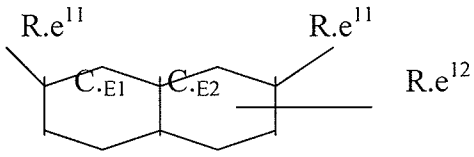
wherein at least one or all free ring atom or their substituents comprise a linking site or functionality J as hereinbefore defined

each spiro ring optionally comprises zero or one or more heteroatoms h

or  (h) comprises zero or 1 N heteroatom and  5,6(h) comprises zero, 1 or 2 N heteroatoms and is unsaturated or comprises one or two –C=C- or -C=N- groups;

and wherein each ring is optionally substituted by one or more oxo, CO, COOH, C_{1-6} alkyl or linear or cyclic alkoxy optionally substituted by one or more oxo, CO, COOH, CN, or C_{1-6} alicyclic or amine groups, amine or one or more spiro or fused heterocycles;

or Lig.e is of the formula Lig.e^3

Lig.e^3 

wherein at least one or all of Re^{11} to Re^{12}, or a ring C or heteroatom or ring substituent comprise a linking site or functionality J as hereinbefore defined

each of $C._{E1}$ and $C._{E2}$ is independently selected from C_{5-6} aryl, heteroaryl, cyloalkyl and heterocyclic, including phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring –C=C- group;

each of up to seven $R.e^{11}$ is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo =O, or cyano, OCH_3, $CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

or any two or more of $R.e^{11}$ form a one, two or three ring fused cyclic structure, a fused 3 ring aryl, 5-heterocyclic or 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic Lig.e^3 structure;

and $R.e^{12}$ is a moiety as defined for $R.e^{11}$ above;

L.e comprises a linking site or functionality J as hereinbefore defined and is suitably as hereinbefore defined for L.a.

56. (Cancelled).

57. (Withdrawn-currently amended) Library as claimed in Claim ~~56~~ 47 wherein Fl is of formula $J_T - t - Fl$ and comprises a BODIPY ™ structure characterised by a dipyrrometheneboron difluoride core, optionally modified by one or two fused rings, optionally substituted by one or several substituents selected from alkyl, alkoxy, aryl or heterocyclic, wherein one substituent –t- is adapted for linking as hereinbefore defined to a ligand precursor as hereinbefore defined, wherein the substituent –t- comprises a proximal unsaturated or aryl moiety, comprising a medial short, medium or long chain alkynyl or cycloalkyl moiety and comprising a moiety derived from linking via a reactive group as hereinbefore defined or selected from carboxyl, sulphonate or as a heteroatom O or S or methylene derived from linking at an alkylhalide including methylbromide, haloacetamide or sulphonate ester electrophilic group.

58. (Cancelled).

59. (Withdrawn-Previously Presented) Process for the preparation of a library as claimed in Claim 47 which is a combinatorial process; and comprises the reaction of one or more ligand precursors of formula IV and/or IV'

IV $(LigJ_L)_m - L - Y_{Lm}$

IV' $Lig\ Y_{Ligm}$

comprising one or more or different reactive groups Y_L or Y_{Lig} forming a linking functionality J, J_L or J_T as hereinbefore defined

with one or more of a plurality of analytical tagging substrates of formula V and/or V'

V Y_{Tm} Tag

V' Y_{Tm} L $(J_T Tag)_m$

comprising one or more or different reactive groups Y_T forming a linking functionality J or J_T as hereinbefore defined

and optionally one or more linking species VI or VI' or VI''

VI Y_{Lm}L Y_{Lm}

wherein Lig, J, L, J_T and Tag and each m is independently as hereinbefore defined

wherein the or each compound of formula IV or IV' is capable of reaction with the or each compound of formula V or V', optionally via the or each species VI or VI' or VI'' to form a plurality of compounds of formula I as hereinbefore defined;

wherein linking is at same or different reactive sites in different compounds as hereinbefore defined.

60. (Withdrawn-Previously Presented) Process for the preparation of a compound of formula I as hereinbelow defined in Claim 64 comprising the reaction of a compound of formula IV or IV' and a compound of formula V or V' and optionally additionally VI, as hereinbefore defined in claim 59.

61-62. (Cancelled).

63. (Withdrawn-Previously Presented) Process as claimed in Claim 59 which comprises additionally determining pharmacology for a plurality of or all compounds in the

library in order to enable selecting a compound exhibiting desired pharmacology, whereby the process comprises preparing a preliminary library of compounds, conducting screens to assess binding or inhibition, selecting a compound identified in the screen as having beneficial properties, and modifying or functionalising by nature of moieties or linking location of linking on the basis of the indications from the screen to prepare an optimised library, wherein the molecular pharmacology and photochemistry from the screen feedback into the design of the library.

64. (Currently Amended) A compound of formula I

$(Lig\ J_L)_m\ \ L(J_TTag)_m(J_TL(J_LLig)_m)_p$

or salt thereof wherein an optically active ligand is present as a racemate or as one of its optically active isomers

comprising ligand moiety Lig linked to tag moiety Tag via linker moiety L at linking site or linking functionality J_T and J_L

wherein Lig ~~comprises a GPCR ligand an inhibitor of an intracellular enzyme or a substrate or inhibitor of a drug transporter~~ is a ligand selected from a non-peptide GPCR ligand agonist and a non-peptide GPCR ligand antagonist, wherein the Lig comprises pharmacological activity as an agonist or antagonist or GPCR receptor binding and activation or inhibition~~;~~

L is selected from ~~a single or double bond, -O-, -S-,~~ amine, ~~COO-,~~ amide, ~~-NN- hydrazine; and~~ saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}600}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P,

wherein optional substituents are selected from any $C_{1\text{-}20}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano and carbonyl and combinations thereof, and L ~~may be~~is monomeric, oligomeric having oligomeric repeat of 2 to 30 or polymeric having polymeric repeat in excess of 30 up to 300;

m are each independently selected from a whole number integer from 1 to 3;

p is 0 to 3

wherein -Tag is a fluorophore entity -Fl, whereby the compound is of formula I'

$(LigJ_L)_m$ L $(J_T\ Fl)_m$ $(J_T$ L $(J_L Lig)_m)_p$

~~characterised in that~~wherein Fl is selected from a red, near ir or blue dye and

the compound of formula I or I' retains pharmacological activity as a fluorescent GPCR ligand agonist or fluorescent GPCR ligand antagonist ~~o~~for GPCR receptor binding and activation or inhibition.

~~with the proviso that:~~

~~a) when Lig is XAC (xanthine amine congener, 8-[4-[(2-aminoethyl)-aminocarbonylmethyloxy]phenyl]-1,3-dipropylxanthine) ie in Lig.a when each of R.a^1 and R.a^2 is propyl, R.a^3 is H and R.a^4 is Ph-OCH$_2$CONH(CH$_2$)$_2$NH-, and L is a single bond Fl is not BODIPY ™ 630/650-X 6-(((4,4-difluoro-5-(2-thienyl)-4-bora-3a,4a-diaza-*s*-indacene-3-yl)styryloxy)acetyl)aminohexanoyl; or~~

~~b) when Lig is ABEA N6-(4-Aminobutyl)-5'-ethylamino-5'-oxo-5'-deoxyadenosine, ie m is 4 and L is a single bond Fl is not BODIPY™ 630/650-X 6-(((4,4-difluoro-5-(2-thienyl)-4-bora-3a,4a-diaza-*s*-indacene-3-yl)styryloxy)acetyl)aminohexanoyl~~.

65. (Previously Presented) A compound of formula I as defined in Claim 64 which is a compound of formula II or III

II $(LigJ_L)_m$ L J_T TagJ_T L $(J_L$ Lig$)_m$ where each m is as hereinbefore defined and is preferably 1 or 2, more preferably 1

III $(LigJ_L)_m$ L $(J_T Tag)_m$ wherein each m is as hereinbefore defined and is preferably 1 and/or 2, more preferably

Lig J_L – L – J_L Tag and/or

Lig J_L – L – J_T Tag and/or Lig J_L – L – J_T Tag

$\searrow J_L$ Lig $\searrow J_T$ Tag

and wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers.

66. (Previously Presented) A compound according to Claim 64, wherein Fl is of formula J_T – t – Fl and comprises a BODIPY ™ structure 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene-3-yl characterised by a dipyrromethene boron difluoride core, optionally modified by one or two fused rings, optionally substituted by one or several substituents selected from alkyl, alkoxy, aryl or heterocyclic, wherein one substituent –t- is adapted for linking as hereinbefore

defined to a ligand precursor as hereinbefore defined, wherein the substituent –t- comprises a proximal unsaturated or aryl moiety, comprising a medial short, medium or long chain alkynyl or cycloalkyl moiety and comprising a moiety derived from linking via a reactive group as hereinbefore defined or selected from carboxyl, sulphonate or as a heteroatom O or S or methylene derived from linking at an alkylhalide including methylbromide, haloacetamide or sulphonate ester electrophilic group.

67. (Withdrawn-Currently Amended) A compound of the formula I or I' as hereinbefore defined in Claim ~~55~~ 64 selected from formulae Lig.a_m L.a-Fl.a_n to Lig.e_m L.eFl.e_n ~~as hereinbefore defined~~

~~with the proviso that:~~

~~a) when Lig is XAC ie in Lig.a when each of R.a^1 and R.a^2 is propyl, R.a^3 is H and R.a^4 is Ph-OCH$_2$CONH(CH$_2$)$_2$NH-, and L is a single bond Fl is not BODIPY™ 630/650 X; or~~

~~b) when Lig is ABEA, ie m is 4 and L is a single bond Fl is not BODIPY™ 630/650 X.~~

wherein:

Lig.a_m is suitably of the formula, in either of the following forms given, including any of its possible linking configurations or sites:

Lig.a $^{1}_{m}$

Wherein at least one or all of Ra^1 to Ra^4, X^1 and X^2 comprise a linking site or functionality J as hereinbefore defined

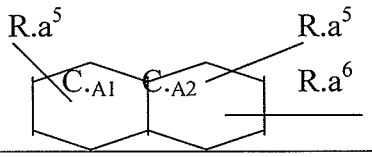
X^1 and X^2 are each independently selected from H, O, OR.a, NR.a, NHR.a;

X^1 and X^2 are each preferably O;

each of $R.a^1$, $R.a^2$, $R.a^3$ and $R.a^4$ independently is selected from H or C_{1-4} linear or branched alkyl optionally mono or multi hydroxy or halo substituted;

$R.a^4$ is selected from a heteroatom O, S or substituted or unsubstituted amine or saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo and cyano; including optionally substituted aryl, cycloalkyl, alkyl, ketone, (di)amine, (di)amide, alkoxy, cycloalkyl, carboxylic acid or optionally o-, m- or p- substituted phenyl wherein substituents include aryl, alkyl, cycloalkyl, heteroaryl or heteroalkyl, amine, amide, carboxyl, carbonyl or $R.a^4$ comprises cyclohexyl, cyclopentyl, ethoxy, $(CH_2)_2PhPh$, CH_2Ph, $CONH(CH_2)nCONH$, $CH_2CONH(CH_2)_2NH$, $CH_2PhNHCOCH_2$, $CH_2CH_2OCOCH_2$, succinimidyl ester, $NHCOCH_2$, $CH_2(CH_3)NCOCH_2$, $H_2N(CH_2)_2NHCOCH_2$, $H_2N(CH_2)_8NHCOCH_2$, $H_2NNHCOCH_2$, $CH_2CONH(CH_2)_2NHCOCH_2$, $HOPhCH_2N(CH_2CH_3.HOAc)(CH_2)_2NHCOCH_2$, heterocyclic-$(CH_2)_4CONH(CH_2)_2NHCOCH_2$ or heterocyclic-$NHCON(heterocyclic)COCH_2$;

or Lig.a is of the formula Lig.a^2-

Lig.a^2 

wherein at least one or all of Ra^5 to Ra^6, or a cyclic C or heteroatom comprise a linking site or functionality J as hereinbefore defined, each of $C._{A1}$ and $C._{A2}$ is independently selected from C_{5-6} aryl, heteroaryl, cycloalkyl and heterocyclic, more preferably from phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring –C=C- group;
Each of up to seven $R.a^5$ is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from H, halo, hydroxy, thiol, amine, COOH, hydrazine, cyano, saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo =O or cyano; OCH_3, $CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

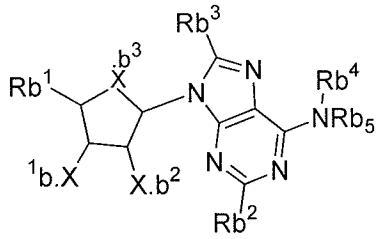
or any two or more of $R.a^5$ form a one, two or three ring fused cyclic structure, a fused 3 ring aryl, 5-heterocyclic or 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic $Lig.a^2$structure;

and $R.a^6$ is a moiety as defined for $R.a^5$ above;

and L.a is as hereinbefore defined for L or J_L L J_T or L.I or subformulae as hereinbefore defined, or is ~~a single bond,~~ amino acid or amide including a peptide or polypeptide gly or gly_3, alkyl of formula $-(CH_2)_n$ where n is 3 to 8, optionally including one or more heteroatoms or unsaturated groups, including –O- or –S- or –CH=CH-:

Lig.b is suitably of the formula Lig.b including any of its possible linking configurations or sites:

Lig.b



wherein at least one or all of Rb^1 to Rb^5 or Xb^1 to Xb^3 comprise a linking site or functionality J as hereinbefore defined

ring substituents $X.b^1$ and $X.b^2$ are independently selected from hydrocarbon including alkyl or SR_X, $NR_{X.2}$ and OR_X wherein (each) R_X is selected from H, C_{1-5}alkyl, alkenyl;

ring heteroatom $X.b^3$ is selected from –S-, -O- and $–CH_2$-;

Rb^1 is selected from saturated or unsaturated, substituted or unsubstituted C_{1-4} aliphatic, or C_{1-3} alicyclic optionally including one or more heteroatoms N, O, S, P, wherein substituent(s) are selected from one or more cycloalkyl, heterocyclic, hydroxy, oxo, halo, amine; or $R.b^1$ comprises a carbonyl substituted by H, alkyl or a linear or cyclic primary, secondary or tertiary amine, substituted C_{1-3} alkyl, cycloalkyl or amide, cyclopropyl, or $CONHC_{1-3}$alkyl including CONHEt or CH_2OH

and each of $R.b^2$ and $R.b^3$ is selected from H, halo, hydroxy, thiol, amine, COOH, CHO, hydrazine, cyano or saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano, preferably from H, halo or hydroxy;

Rb^4 is H;

Rb^5 is H or alkyl

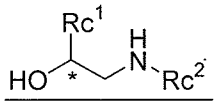
L.b comprises a linking site or functionality J as hereinbefore defined; and

is as hereinbefore defined for L or its subformulae, more preferably is saturated and unsaturated substituted or unsubstituted C_{1-12} aliphatic or C_{1-24} aromatic as

defined for L optionally including one or more heteroatoms O, S or N, cyclic or heterocyclic groups, or is of formula L.I or its subformulae as hereinbefore defined, or is $(CH_2)m$ wherein m is 2 to 12, or is $(Ph\text{-}CH_2CONH)_2\ (CH_2)_2$;

Lig.c is of the formula Lig.c including any of its possible linking configurations or sites:

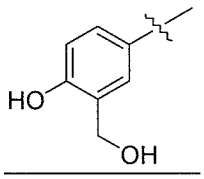
Lig.c $HOC^*(R.c^1)CH_2NH\text{-}R.c^2$



where at least one or all of Rc^1 to Rc^2 or OH, or a chain C or N comprise a linking site or functionality J as hereinbefore defined

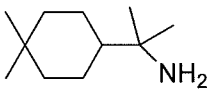
* indicates an optically active centre and

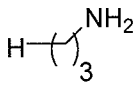
wherein $R.c^1$ is $C_{6\text{-}14}$ aryl optionally including one or more heteroatoms selected from H, O, optionally substituted by OH, Hal, NH_2, $NHC_{1\text{-}3}$alkyl, sulphonamide, oxoamine or $(\text{-}CONH_2)$, or is mono, di or tri substituted phenyl or quinoline wherein substituents include OH, Cl or NH_2, or is m-CH_2OH, p-OH phenyl, m-,p-dihydroxy phenol or m-,m-dihydroxyphenol, m-,m-diCl, p-NH_2 phenol, p-OH, m-$CONH_2$ phenol or 5-OH, 8-quinoline,



$R.c^2$ is selected from saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}20}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any optionally substituted $C_{1\text{-}12}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine,

oxo or cyano and combinations thereof; or R.c^2 is selected from C_{1-6} branched or straight chain aliphatic, C_{6-10} araliphatic optionally substituted by OH and optionally including heteroatoms selected from N,O, optionally including an ether O, and is selected from $-(CH_2)_6OCH((CH_2)_3Ph)$, $CHCH_3(CH_2)_2Ph$, $CHCH_3CH_2PhOH$, $C(CH_3)_2CH_2Ph$ or from the structures:

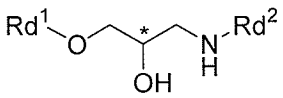




L.c is present as R.c^2 or comprises a linking site or functionality J as hereinbefore defined, and is as hereinbefore defined for L, formula L.I or its subformulae as hereinbefore defined, or is selected from C_{1-12} alkyl, amide;

Lig.d is of the formula Lig.d including any of its possible linking configurations or sites:

Lig.d R.d^1 $OCH_2C^*HOHCH_2NH$-R.d^2

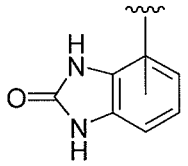


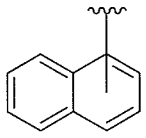
where at least one or all of Rd^1 to Rd^2 or OH, a chain C or N comprise a linking site or functionality J as hereinbefore defined

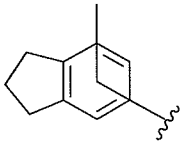
* indicates an optically active centre

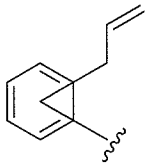
wherein R.d^1 is saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano; or R.d^1 is substituted or unsubstituted C_{1-24} aralkyl or heteroaralkyl, including single ring and fused ring systems with (hetero)aryl or cycloalkyl rings, wherein optional

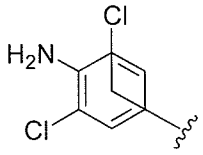
substituents include C_{1-6} alkyl, alkoxy, ether, carbonyl, alkenyl, amine, amide each optionally carbonyl, amide, halo or OH substituted, or halo or OH, amine, amide, carbonyl, ketone, ether substituted phenyl or naphthyl, mono-, di-, tri- or tetra substituted mono or polycyclic fused aryl or cycloaryl or heterocycloaryl including phenyl, carbazole or structures shown below or spiro ring systems, mono-, di-, tri- or tetra alkoxyalkyl, alkoxyalkoxyalkyl or CF_3 substituted phenyl or unsubstituted or monosubstituted naphthalene or 5,6 ring systems:



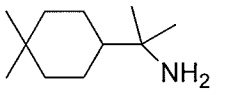
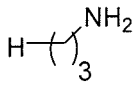
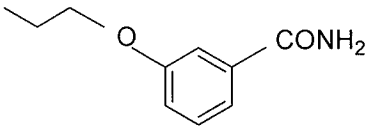
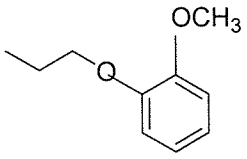








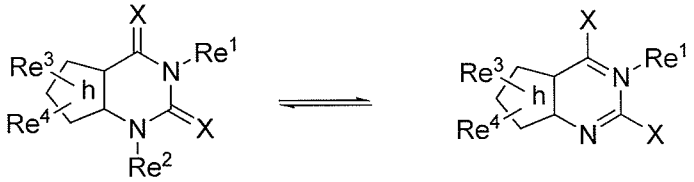
R.d^2 is substituted or unsubstituted amine, saturated or unsaturated, substituted or unsubstituted C_{1-12} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano, more preferably amine, C_{1-6} branched or straight chain alkyl optionally including ether O, and optionally substituted by C_{6-10} aryl, or of the formula:

L.d may be present as $R.d^2$ or may comprise a linking site or functionality J as hereinbefore defined and is as hereinbefore defined for L and its subformulae , formula L.I and its subformulae as hereinbefore defined, or is ~~a single bond or is~~ as hereinbefore defined for L.a;

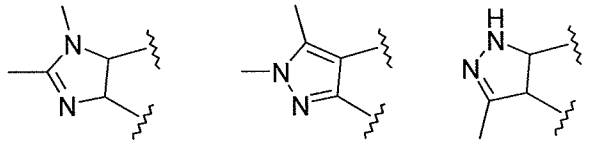
Lig.e comprises a cell permeant moiety or is associated with a cell permeant L or Fl moiety or is of the formula , in either of the following forms given including any of its possible linking configurations or sites:

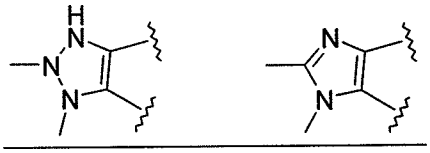
Lig.e^1



wherein at least one or all of Re^1 to Re^4, X and a ring C or N comprise a linking site or functionality J as hereinbefore defined

h is selected from





each optionally substituted by R.e^3 – R.e^4 wherein R.e^1 – R.e^4 are as R.a^1 – R.a^4 defined above or in which R.e^3 is C_{5-9} linear or branched alkyl, optionally mono or multi hydroxy or halo substituted or is aryl optionally substituted by alkoxy or sulfonyl,

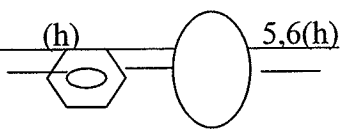
ortho-OEt, meta-SO_2N  NCH_3

each X is independently selected from H, O, -OR.e^2, N, HN, NR.e^5, HR.e^6 , and aryl optionally substituted by ether; or X is aryl optionally alkyl or alkoxy substituted or is Ph-ortho-$OCH_2CH_2CH_3$;

and where R.e^5 is as defined above for R.e^1 above or forms a fused cyclic ring together with the adjacent ring N atom, or 1 or 2 fused 5 membered cyclic rings;

and R.e^6 is as defined above for R.e^1 above or is selected from optionally substituted phenyl wherein optional substituents include ether, o-ethoxy or o-propoxy, alkyl or OH, sulphonyl or carbonyl substituted by heterocyclic, or cyclic C_{5-8} alkyl, piperazinyl or sulphonyl;

or Lig.e is of the formula Lig.e^2

Lig.e^2 

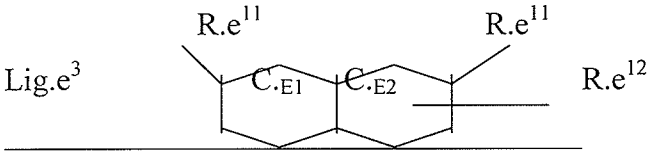
wherein at least one or all free ring atom or their substituents comprise a linking site or functionality J as hereinbefore defined

each spiro ring optionally comprises zero or one or more heteroatoms h

or (h)  comprises zero or 1 N heteroatom and  5,6(h) comprises zero, 1 or 2 N heteroatoms and is unsaturated or comprises one or two –C=C- or -C=N- groups;

and wherein each ring is optionally substituted by one or more oxo, CO, COOH, C_{1-6} alkyl or linear or cyclic alkoxy optionally substituted by one or more oxo, CO, COOH, CN, or C_{1-6} alicyclic or amine groups, amine or one or more spiro or fused heterocycles;

or Lig.e is of the formula $Lig.e^3$



wherein at least one or all of Re^{11} to Re^{12}, or a ring C or heteroatom or ring substituent comprise a linking site or functionality J as hereinbefore defined

each of $C._{E1}$ and $C._{E2}$ is independently selected from C_{5-6} aryl, heteroaryl, cyloalkyl and heterocyclic, including phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring –C=C- group;

each of up to seven $R.e^{11}$ is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo =O, or cyano, OCH_3,

$CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

or any two or more of $R.e^{11}$ form a one, two or three ring fused cyclic structure, a fused 3 ring aryl, 5-heterocyclic or 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic $Lig.e^3$ structure;

and $R.e^{12}$ is a moiety as defined for $R.e^{11}$ above;

L.e comprises a linking site or functionality J as hereinbefore defined and is suitably as hereinbefore defined for L.a.

68. (Currently Amended) A compound of the formula I

$(Lig\,J_L)_m\;\; L(J_TTag)_m(J_TL(J_LLig)_m)_p$

or salt thereof and salts thereof wherein an optically active ligand is present as a racemate or as one of its optically active isomers

comprising ligand moiety Lig linked to tag moiety Tag via linker moiety L at linking site or linking functionality J_T and J_L

wherein Lig ~~comprises a GPCR ligand, an inhibitor of an intracellular enzyme or a substrate or inhibitor of a drug transporter~~ is a ligand selected from a non-peptide GPCR ligand agonist and a non-peptide GPCR ligand antagonist, wherein the Lig comprises pharmacological activity as an agonist or antagonist ~~o~~for GPCR receptor binding and activation or inhibition;

L is selected from ~~a single or double bond, O, S,~~ amine, ~~COO,~~ amide, ~~NN hydrazine; and~~ saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}600}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P,

wherein optional substituents are selected from any C_{1-20} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano and carbonyl and combinations thereof, and L may be monomeric, oligomeric having oligomeric repeat of 2 to 30 or polymeric having polymeric repeat in excess of 30 up to 300;

m are each independently selected from a whole number integer from 1 to 3;

p is 0 to 3

wherein -Tag is a fluorophore entity -Fl, whereby the compound is of formula I'

$(LigJ_L)_m$ L $(J_T\ Fl)_m$ $(J_T$ L $(J_L Lig)_m)_p$

wherein Fl is selected from the class of dyes including TEXAS RED™ sulforhodamine 101 acid chloride, coumarin and derivatives, CASCADE BLUE™ pyrenyloxytrisulfonic acid, EVOBLUE™ oxazine based dyes and fluorescent derivatives thereof, pyrenes and pyridyloxazole derivatives, the cyanine dyes, the dyomics (DY dyes and ATTO dyes) and fluorescent derivatives thereof, the Alexafluor dyes and derivatives, BDI dyes including the commercially available Bodipy™ 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene-3-yl dyes, pyrenes, anthracenes, acridines, fluorescent phycobiliproteins and their conjugates and fluoresceinated microbeads, and TEXAS RED™ sulforhodamine 101 acid chloride derivatives, coupled to amine groups using the isocyanate, succinimidyl ester or dichlorotriazinyl-reactive groups

and the compound of formula I or I' retains pharmacological activity as a fluorescent GPCR ligand agonist or fluorescent GPCR ligand antagonist ~~o~~for GPCR receptor binding and activation or inhibition.

~~and~~

~~wherein the compound of formula I is selected from a GPCR ligand having agonist properties and a GPCR ligand having antagonist properties,~~

~~with the proviso that~~

~~a) when Lig is XAC (xanthine amine congener, 8-[4-[(2-aminoethyl)-aminocarbonylmethyloxy]phenyl]-1,3-dipropylxanthine) ie in Lig.a when each of R.a^1 and R.a^2 is propyl, R.a^3 is H and R.a^4 is -Ph-OCH$_2$CONH(CH$_2$)$_2$NH-, and L is a single bond Fl is not BODIPY ™ 630/650-X 6-(((4,4-difluoro-5-(2-thienyl)-4-bora-3a,4a-diaza-*s*-indacene-3-yl)styryloxy)acetyl)aminohexanoyl; or~~

~~b) when Lig is ABEA N6-(4-Aminobutyl)-5'-ethylamino-5'-oxo-5'-deoxyadenosine, ie m is 4 and L is a single bond Fl is not BODIPY™ 630/650-X 6-(((4,4-difluoro-5-(2-thienyl)-4-bora-3a,4a-diaza-*s*-indacene-3-yl)styryloxy)acetyl)aminohexanoyl~~.

69. (Withdrawn and Currently Amended) A kit comprising a Compound of formula I or I' as hereinbefore defined in Claim 47 associated with information relating to its pharmacological properties in the form of Spectral Properties given as Excitation Max and Emission Max, Fluorescence Lifetime and Emission quantum yield and Pharmacology defined in terms of cells expressing a GPCR receptor as hereinbefore defined ~~or expressing an intracellular cyclic nucleotide phosphodiesterase, or a drug transporter as hereinbefore defined~~ and given as the Inhibition or Antagonism of receptor binding or of receptor functionality together with a value for the Inhibition (pK_B) or Antagonism (pK_I) binding constants, and optionally together with fluorescent images of the pharmacological binding in single living cells illustrating the

defined inhibition or antagonism, preferably the pharmacological properties are given as EC_{50} values for agonist stimulated – or pK_i values for antagonism of agonist stimulated second messenger generation~~, or substrate K_m values or antagonist K_i values for stimulation or inhibition of intracellular enzymes or drug transporters~~.

70. (Withdrawn-Previously Presented) Compound of formula IV or IV' or library thereof as hereinbefore defined in Claim 59.

71. (Withdrawn-Previously Presented) Fluorophore linker of formula V' or library thereof as hereinbefore defined in Claim 59.

72. (Withdrawn-Currently Amended) Kit comprising ligand precursors, linker precursors and tag precursors of formulae IV, IV', V, V' and/or VI as hereinbefore defined in Claim 59 for preparing a library of compounds of formula I $(Lig\ J_L)_m\ L(J_T Tag)_m(J_T\ L(J_L Lig)_m)_p$ and salts thereof wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers

comprising one or a plurality of same or different ligand moieties Lig each linked to one or a plurality of same or different tag moieties Tag via same or different linker moieties L and same or different linking site or linking functionality J_T and J_L

wherein Lig ~~comprises a GPCR ligand, an inhibitor of an intracellular enzyme or a substrate or inhibitor of a drug transporter~~ is a ligand selected from a non-peptide GPCR ligand agonist and a

non-peptide GPCR ligand antagonist, wherein the Lig comprises pharmacological activity as an agonist or antagonist or GPCR receptor binding and activation or inhibition;

L is selected from ~~a single or double bond, -O-, -S-,~~ amine, ~~COO-,~~ amide, ~~-NN-hydrazine; and~~ saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}600}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, wherein optional substituents are selected from any $C_{1\text{-}20}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano and carbonyl and combinations thereof, and L ~~may be~~is monomeric, oligomeric having oligomeric repeat of 2 to 30 or polymeric having polymeric repeat in excess of 30 up to 300;

Tag is any tagging substrate;

m are each independently selected from a whole number integer from 1 to 3;

p is 0 to 3

wherein one or more of each -Tag in one or more or each library compound is a fluorophore entity -Fl, whereby the library comprises compounds of which one or more or all of which compounds are of formula I'

$(LigJ_L)_m$ $L(J_TFl)_m(J_T\ L(J_LLig)_m)_p$

wherein linking is at same or different linking sites in compounds comprising different Lig, J_L, L J_T and/or – Tag and is at different linking sites in compounds comprising same Lig, J_L, L J_T and/or – Tag

wherein the or each Fl is selected from a red, near ir or blue dye and

and the compound of formula I or I' retains pharmacological activity as a fluorescent GPCR ligand agonist or fluorescent GPCR ligand antagonist for GPCR receptor binding and activation or inhibition.

73. (Withdrawn-Previously Presented) A library of fluorescent ligands of formula I or I' or a compound thereof as hereinbefore defined in Claim 47 for visualising receptors or receptor binding, assessing pharmacological properties of the fluorescent ligand, in high throughput screening of novel chemical entities that bind to the target receptor, in inhibiting an intracellular enzyme or inhibiting a drug transporter or a substrate of a drug transporter, in studying drug transport or drugs suitable for transport or in distinguishing healthy or diseased tissue.

74. (Withdrawn-Currently Amended) A library of fluorescent ligands of formula I or I' or a compound thereof as hereinbefore defined in claim 47 or 64 for use in a method for GPCR receptor binding or inhibition, ~~intracellular enzyme inhibition or drug transport or inhibition~~ and visualisation comprising contacting the library or a compound thereof with a sample comprising live cell material comprising GPCRs, ~~intracellular enzymes or drug transporters~~ in manner to facilitate binding ~~or inhibition~~ thereof ~~or transport thereby~~, and detecting changes in fluorescence or location thereof.

75. (Withdrawn-Previously Presented) A library of fluorescent ligands of formula I or I' or a compound thereof for use as claimed in claim 74 wherein the library or compound thereof is a fluorescent ligand(s) which has affinity such that it binds semi-permanently or transiently and remains bound when unbound ligand is washed away.

76. (Withdrawn-Previously Presented) A library of fluorescent ligands of formula I or I' or a compound thereof for use as claimed in claim 74 wherein detecting a change in fluorescence is by means of confocal microscopy or fluorescence correlation spectroscopy.

77. (Withdrawn-Previously Presented) A library of fluorescent ligands of formula I or I' or a compound thereof for use as claimed in claim 74 wherein the library or compound thereof comprises fluorescent ligand agonist(s) which maintains its binding affinity and functional activity or is an antagonist which maintains its binding affinity on linking or when linked to fluorescent moiety Fl.

78. (Withdrawn-Currently Amended) A kit comprising a library or a compound of formula I or I' as claimed in claim 47 or 64 and a target therefor provided as cell derived material selected from a cell line, expressing a GPCR, ~~intracellular enzyme or drug transporter,~~ membrane containing these proteins derived from such a cell line, solubilised receptor, ~~enzyme or drug transporter~~ or GPCR array from that cell line.

79. (Withdrawn-Currently Amended) Kit as claimed in Claim 78 wherein the cell derived material is provided in one of three forms: (1) from cells expressing a green fluorescent protein tagged receptor, ~~intracellular enzyme or drug transporter;~~ (2) from cells expressing an epitope tag for a commercially available fluorescent antibody or (3) a wild-type protein for which a specific fluorescent antibody is also provided.

80-82. (Cancelled).

83. (Withdrawn-Currently Amended) Library as claimed in Claim 55 wherein: Lig.a comprises linking functionality J_L which is amine, and is of the formula, in either of the following forms given:

Lig.a $^{1}{}_{m}$

wherein Ra^4 comprises linking functionality J_L and J_T which is amine;

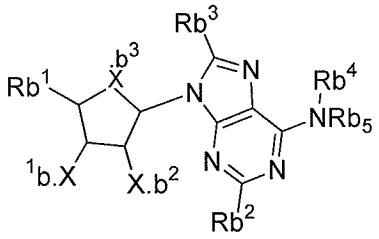
X^1 and X^2 are each O;

$R.a^3$ is H;

each of $R.a^1$ and $R.a^2$ is n-propyl;

R.a^4 is p- substituted phenyl wherein the substituent is heteroalkyl amide amine; and includes L which is ~~a single bond or is~~ C_{1-50} alkyl optionally substituted by C_1 alkyl and including the formula $-(CH_2)_n$ where n is 3 to 8, optionally including one or more heteroatoms –O;

Lig.b comprises linking functionality J_L which is amine, and is



wherein ring substituents X.b^1 and X.b^2 are each OH;

ring heteroatom X.b^3 is -O- ;

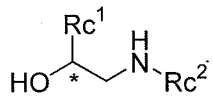
Rb^1 is CONHEt or CH_2OH;

and each of R.b^2 and R.b^3 is H;

Rb^4 is H;

Rb^5 comprises linking functionality J_T which is amino, and linker L.b selected from saturated C_{1-12} aliphatic and C_{6-24} aromatic, optionally substituted by one or more C_1 alkyl and optionally including one or more heteroatoms O or cyclic groups;

Lig.c comprises linking functionality J_L which is amine and is

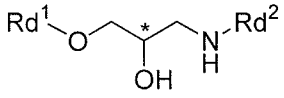


as a racemate or as one of its optically active isomers wherein * indicates an optically active centre,

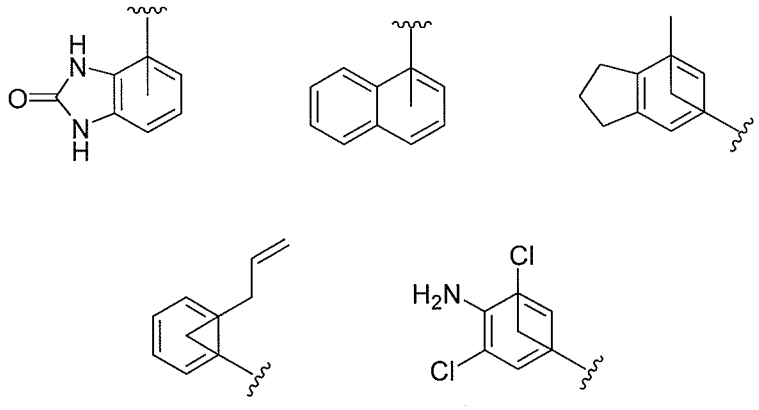
Rc^1 is m-, p- dihydroxyphenyl; and

Rc^2 comprises linking functionality J_T which is amine, and linker L.c which is selected from C_{1-12} straight chain alkyl, C_{6-12} cycloalkyl or aryl and combinations thereof optionally comprising one or more heteroatoms O and optionally substituted by C_1 aliphatic;

or Lig.d comprises a linking functionality J_L which is amine and is



as a racemate or as one of its optically active isomers wherein * indicates an optically active centre,



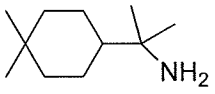
Rd^1 is selected from the structures

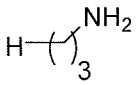
and a substituted C_{1-20} spiro aromatic ring system comprising a single aromatic ring and a heteroaryl and optionally halo substituted; and

Rd^2 comprises linking functionality J_T which is amine, and linker L.d which is selected from C_{1-12} straight chain alkyl, C_{6-12} cycloalkyl or aryl and combinations thereof optionally comprising one or more heteroatoms O and optionally substituted by C_1 aliphatic; or Rd^2 is C_{1-6} straight chain alkyl including ether O and substituted by C_{6-10} aryl which is OH and oxo substituted and comprises linker L.d as hereinbefore defined.

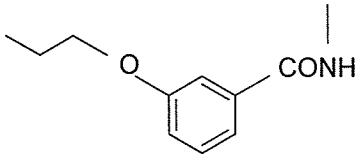
84. (Withdrawn-Currently Amended) Library as claimed in claim 83 wherein $R.a^4$, $R.b^5$ or $R.c^2$ or $R.d^2$ comprises linking functionality J_T which is amino, and linker L.a, L.b, L.c or L.d selected from $(CH_2)m$ wherein m is 3, 4, 6 or 8 or is in the range 3 to 8 or 2 to 12 optionally including one or more substituents C_1, or J_L L J_T is mono or polyethylene glycol diamine~~, or L.a is a single bond~~; or

$R.c^2$ or $R.d^2$ comprises linking functionality J_T which is amino, and linker L.c or L.d selected from $C(CH_3)_2CH_2Ph$ and mono amino menthane or the structure





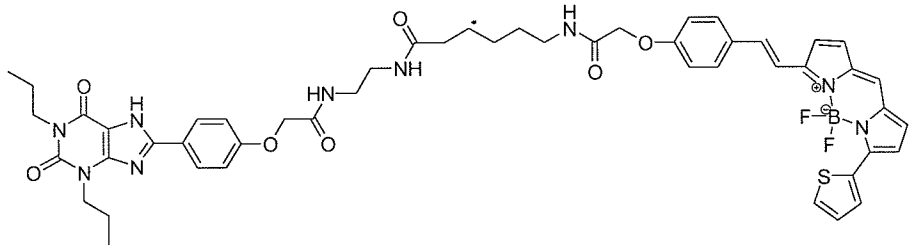
or Rd^2 comprises the following OH substituted aryl structure wherein linking functionality J_L is shown as amine, Ld is as hereinabove defined and includes J_T which is amine:



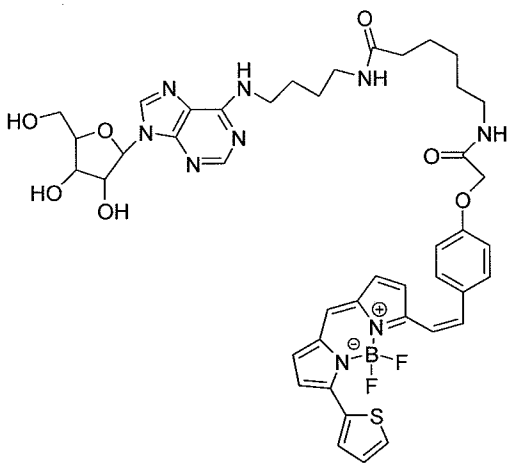
85. (Cancelled).

86. (Withdrawn-Previously Presented) Library as claimed in Claim47 wherein Fl is selected from Texas Red ™, Cy5.5 or Cy5 or analogues thereof, DY-630, DY-640, DY-650 or DY-655 or analogues thereof, ATTO 655 or ATTO 680 or analogues thereof, EvoBlue 30 or analogues thereof, Alexa 647 or analogues thereof, BODIPY 630/650 and analogues thereof including BODIPY 630/650 X.

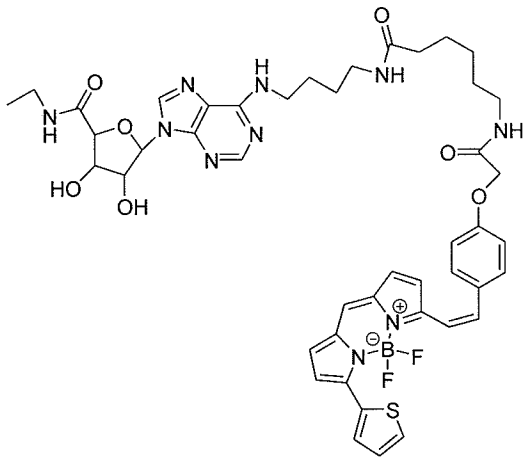
87. (Withdrawn-Currently Amended) Library comprising a compound selected from the following structures wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers:



XAC – BODIPY 630/650 X



ABA-BY630



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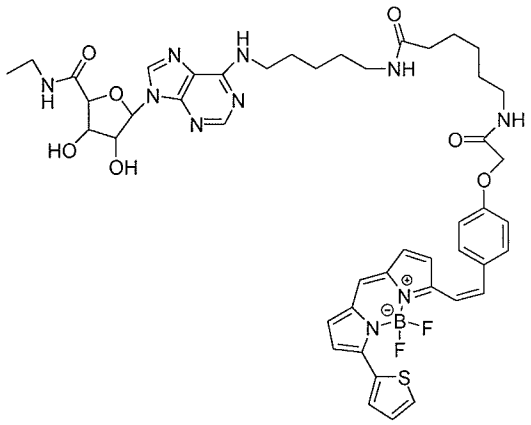
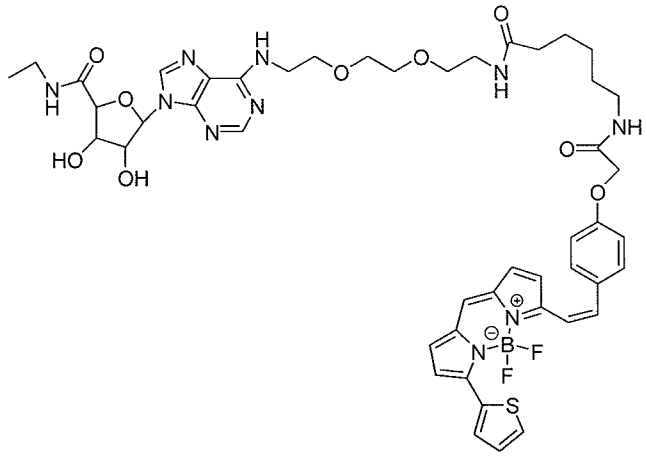
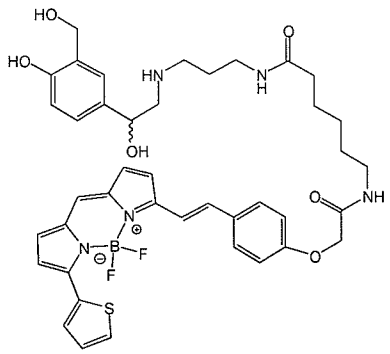


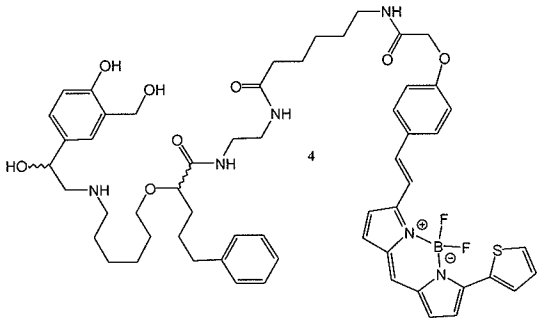
APEA-BY 630



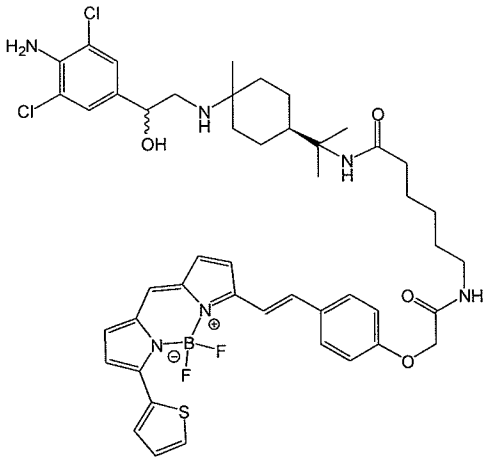
ABIPEA – BY630



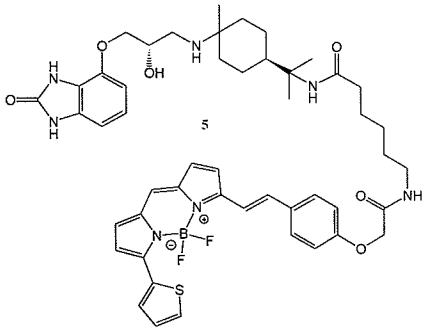
and



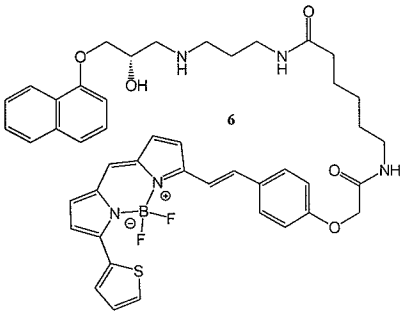
Salmeterol BY 630/650



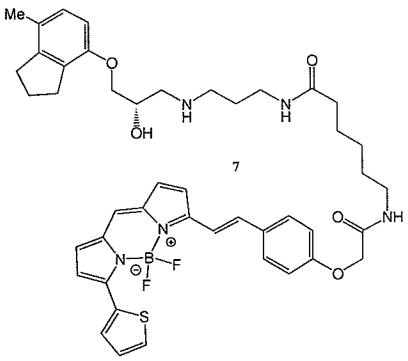
Clenbuterol BY 630/650



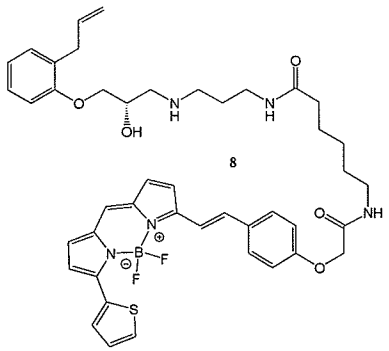
CGP12177-BY 630/650



Propranolol BY630/650



ICI118551-BY630/650



Alprenolol-BY630/650

and wherein the library comprises pharmacological activity as a fluorescent GPCR ligand agonist or fluorescent GPCR ligand antagonist for GPCR receptor binding and activation or inhibition.

88. (Withdrawn-Currently Amended) Compound as claimed in Claim 67 wherein: Lig.a comprises linking functionality J_L which is amine, and is of the formula, in either of the following forms given:

Lig.a $^{1}{}_{m}$

wherein Ra^4 comprises linking functionality J_L and J_T which is amine;

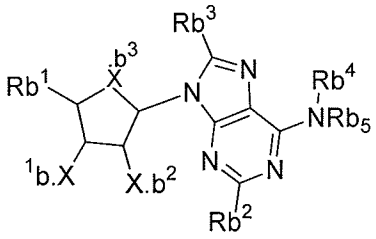
X^1 and X^2 are each O;

$R.a^3$ is H;

each of $R.a^1$ and $R.a^2$ is n-propyl;

$R.a^4$ is p- substituted phenyl wherein the substituent is heteroalkyl amide amine; and includes L which is ~~a single bond or is~~ $C_{1\text{-}50}$ alkyl optionally substituted by C_1 alkyl and including the formula $-(CH_2)_n$ where n is 3 to 8, optionally including one or more heteroatoms –O;

Lig.b comprises linking functionality J_L which is amine, and is



wherein ring substituents $X.b^1$ and $X.b^2$ are each OH;

ring heteroatom $X.b^3$ is -O- ;

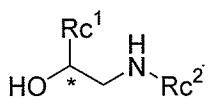
Rb^1 is CONHEt or CH_2OH;

and each of $R.b^2$ and $R.b^3$ is H;

Rb^4 is H;

Rb^5 comprises linking functionality J_T which is amino, and linker L.b selected from saturated $C_{1\text{-}12}$ aliphatic and $C_{6\text{-}24}$ aromatic, optionally substituted by one or more C_1 alkyl and optionally including one or more heteroatoms O or cyclic groups;

Lig.c comprises linking functionality J_L which is amine and is

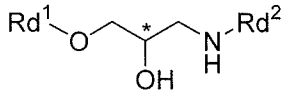


as a racemate or as one of its optically active isomers wherein * indicates an optically active centre,

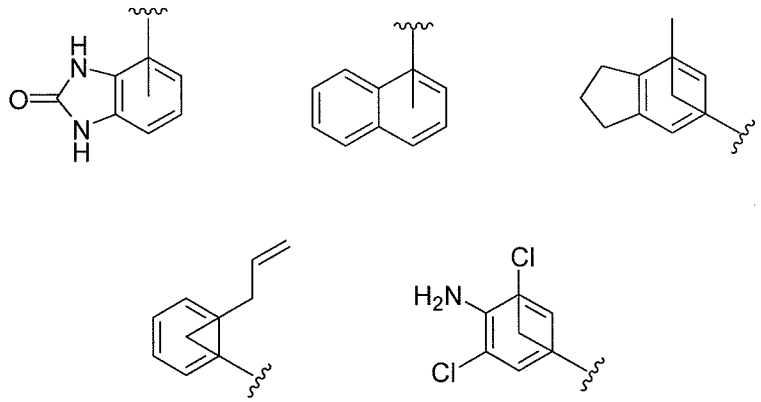
Rc^1 is m-, p- dihydroxyphenyl; and

Rc^2 comprises linking functionality J_T which is amine, and linker L.c which is selected from C_{1-12} straight chain alkyl, C_{6-12} cycloalkyl or aryl and combinations thereof optionally comprising one or more heteroatoms O and optionally substituted by C_1 aliphatic;

or Lig.d comprises a linking functionality J_L which is amine and is



as a racemate or as one of its optically active isomers wherein * indicates an optically active centre,



Rd^1 is selected from the structures

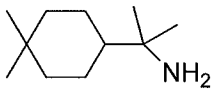
and a substituted C_{1-20} spiro aromatic ring system comprising a single aromatic ring and a heteroaryl and optionally halo substituted; and

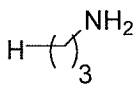
Rd^2 comprises linking functionality J_T which is amine, and linker L.d which is selected from C_{1-12} straight chain alkyl, C_{6-12} cycloalkyl or aryl and combinations thereof optionally comprising one or more heteroatoms O and optionally substituted by C_1 aliphatic; or Rd^2 is C_{1-6} straight chain alkyl including ether O and substituted by C_{6-10} aryl which is OH and oxo substituted and comprises linker L.d as hereinbefore defined,

with the proviso that the compound is not a compound excluded in Claim ~~18~~47.

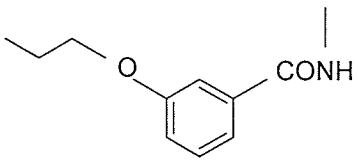
89. (Withdrawn-Currently Amended) Compound as claimed in Claim 88 wherein $R.a^4$, $R.b^5$ or $R.c^2$ or $R.d^2$ comprises linking functionality J_T which is amino, and linker L.a, L.b, L.c or L.d selected from $(CH_2)m$ wherein m is 3, 4, 6 or 8 or is in the range 3 to 8 or 2 to 12 optionally including one or more substituents C_1, or J_L L J_T is mono or polyethylene glycol diamine~~, or L.a is a single bond~~; or

$R.c^2$ or $R.d^2$ comprises linking functionality J_T which is amino, and linker L.c or L.d selected from $C(CH_3)_2CH_2Ph$ and mono amino menthane or the structure





or Rd^2 comprises the following OH substituted aryl structure wherein linking functionality J_L is shown as amine, Ld is as hereinabove defined and includes J_T which is amine:



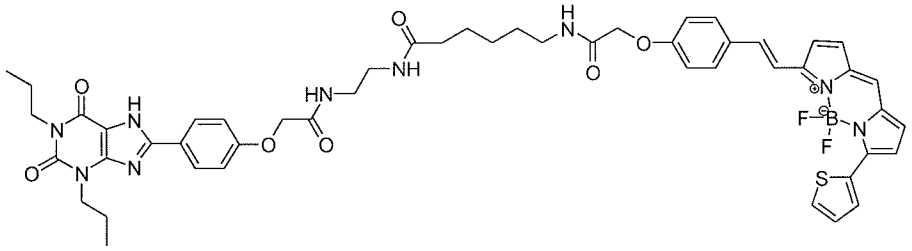
~~with the proviso that when Lig is XAC ie in Lig.a when each of R.a^1 and R.a^2 is propyl, R.a^3 is H and R.a^4 is Ph $OCH_2CONH(CH_2)_2NH$, and L is a single bond Fl is not BODIPY ™ 630/650 X; or~~

~~b) when Lig is ABEA, ie m is 4 and L is a single bond Fl is not BODIPY™ 630/650 X.~~

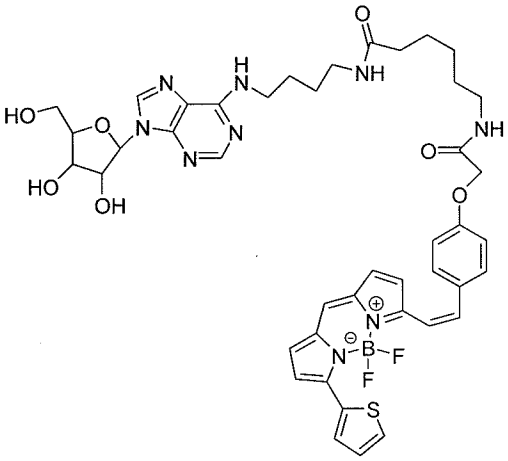
90. (Cancelled).

91. (Previously Presented) Compound as claimed in Claim 64 wherein Fl is selected from TEXAS RED ™ sulforhodamine 101 acid chloride, Cy5.5 or Cy5 or analogues thereof, DY-630, DY-640, DY-650 or DY-655 or analogues thereof, ATTO 655 or ATTO 680 or analogues thereof, EVOBLUE™30 oxazine based dye or analogues thereof, Alexa 647 or analogues thereof, BODIPY™ 630/650 6-(((4,4-difluoro-5-(2-thienyl)-4-bora-3a,4a-diaza-*s*-indacene-3-yl)styryloxy)acetyl and analogues thereof including BODIPY™ 630/650-X 6-(((4,4-difluoro-5-(2-thienyl)-4-bora-3a,4a-diaza-*s*-indacene-3-yl)styryloxy)acetyl)aminohexanoyl.

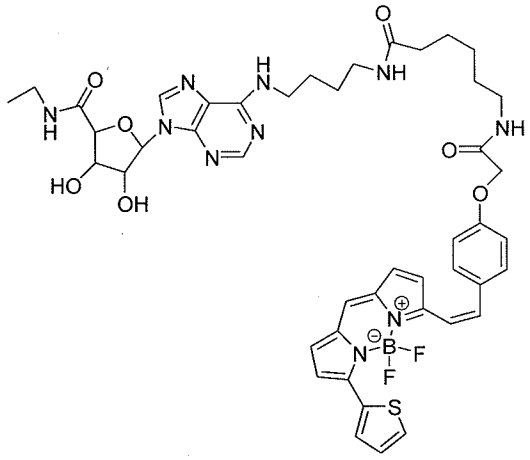
92. (Withdrawn-Currently Amended) Compound as given in ~~selected from~~ the following structures wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers:



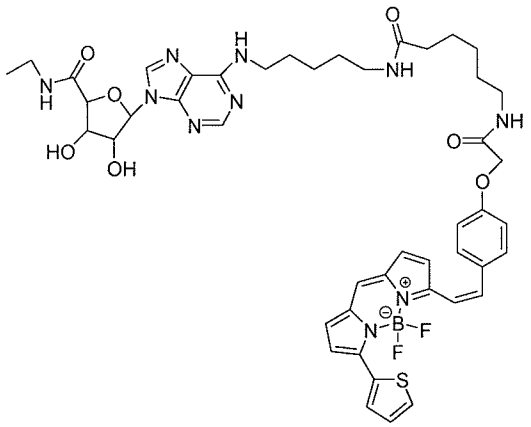
XAC – BODIPY 630/650 X



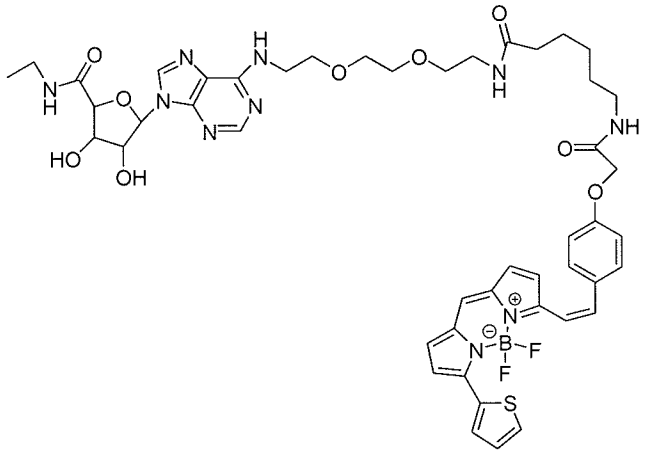
ABA-BY630



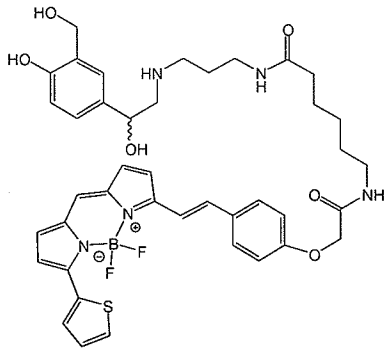
ABEA-BY630



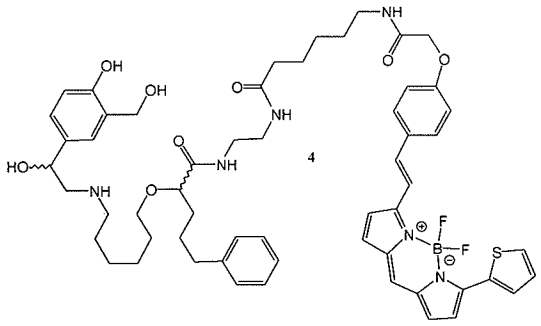
APEA-BY 630



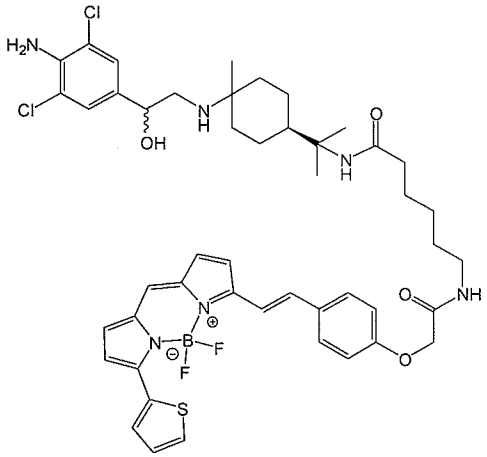
ABIPEA – BY630



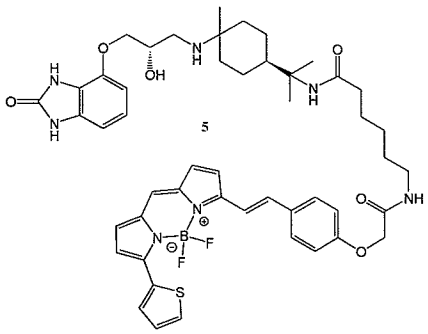
And Salmeterol derivative – BY 630/650



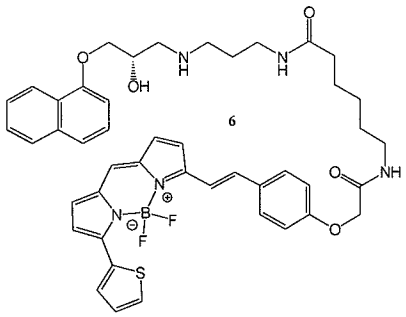
Salmeterol BY 630/650



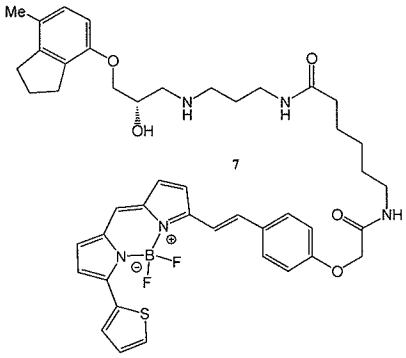
Clenbuterol BY 630/650



CGP12177-BY 630/650



Propranolol BY630/650



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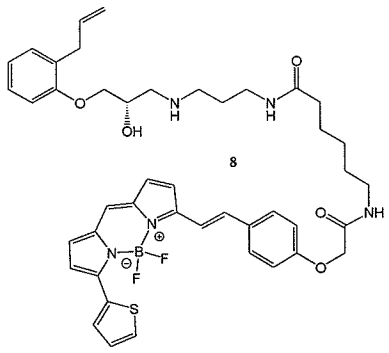


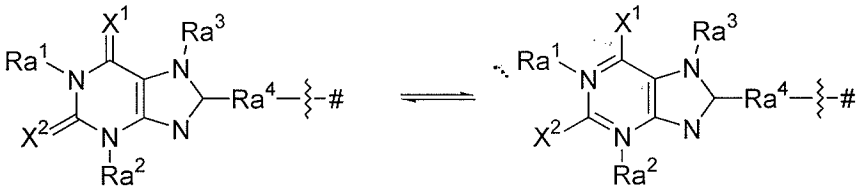
Alprenolol-BY630/650

and wherein the compound comprises pharmacological activity as a fluorescent GPCR ligand agonist or fluorescent GPCR ligand antagonist for receptor binding and activation or inhibition.

93. (Withdrawn-Currently Amended) Library of tagged non-peptide ligands comprising moiety Lig and L selected from formula Lig.a-L.a- - Lig.e-L.e associated with a Tag which is an entity –Fl wherein the or each –Fl is selected from a red, near ir or blue dye and wherein:

Lig.a- is suitably of the formula, in either of the following forms given:

Lig.a [1]-



Wherein X^1 and X^2 are each independently selected from H, =O, OR.a, NR.a, NHR.a;

X^1 and X^2 are each preferably =O;

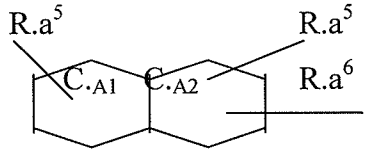
each of R.a, R.a^1, R.a^2 and R.a^3 independently is selected from H or C_{1-4} linear or branched alkyl, preferably H, methyl, ethyl, n-propyl, isopropyl, n-butyl, t-butyl or isobutyl optionally mono or multi hydroxy or halo substituted, such as CH_2OH, CH_2F or $CH_2CHOHCH_2OH$;

R.a^4 is selected from a heteroatom O, S or substituted or unsubstituted amine or saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may

comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like;

preferably R.a^4 is selected from optionally substituted aryl, cycloalkyl, alkyl, ketone, (di)amine, (di)amide, more preferably optionally substituted alkoxy, cycloalkyl, amine, amide, carboxylic acid or optionally o-, m- or p- substituted phenyl wherein substituents include aryl, alkyl, cycloalkyl, heteroaryl or heteroalkyl, amine, amide, carboxyl, carbonyl etc, for example is cyclohexyl, cyclopentyl, ethoxy, $(CH_2)_2PhPh$, CH_2Ph, $CONH(CH_2)nCONH$, $CH_2CONH(CH_2)_2NH$, $CH_2PhNHCOCH_2$, $CH_2CH_2OCOCH_2$, succinimidyl ester, $NHCOCH_2$, $CH_2(CH_3)NCOCH_2$, $H_2N(CH_2)_2NHCOCH_2$, $H_2N(CH_2)_8NHCOCH_2$, $H_2NNHCOCH_2$,$CH_2CONH(CH_2)_2NHCOCH_2$, $HOPhCH_2N(CH_2CH_3.HOAc)(CH_2)_2NHCOCH_2$, heterocyclic-$(CH_2)_4CONH(CH_2)_2NHCOCH_2$, heterocyclic-$NHCON$(heterocyclic)$COCH_2$ and the like;

or Lig.a- is of the formula Lig.a^2-

Lig.a^2 

wherein each of $C._{A1}$ and $C._{A2}$ is independently selected from aryl, heteroaryl, cyloalkyl and heterocyclic, more preferably from phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring –C=C- group;

Each of up to seven $R.a^5$ is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from H, halo, hydroxy, thiol, amine, COOH, hydrazine, cyano, saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}20}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from any $C_{1\text{-}12}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like, such as =O, OCH_3, $CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

or any two or more of $R.a^5$ form a one, two or three ring fused cyclic structure, preferably comprising a fused 3 ring aryl, 5-heterocyclic, 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic $Lig.a^2$structure;

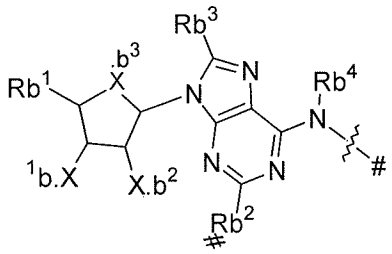
and $R.a^6$ is a moiety as defined for $R.a^5$ above;

and -L.a- is as hereinbefore defined for -L- and is suitably of formula -L.I- or -L.II- as hereinbefore defined, more preferably is selected from ~~a single bond,~~ amino acid or amide such as a peptide or polypeptide for example gly or gly_3, alkyl of formula $–(CH\text{-}_2)_n$ where n is 3 to 8,

preferably 3, 4 or 6, optionally including one or more heteroatoms or unsaturated groups, such as –O- or –S- or –CH=CH- and the like:

Lig.b is suitably of the formula Lig.b

Lig.b



wherein ring substituents $X.b^1$ and $X.b^2$ are independently selected from hydrocarbon such as alkyl or SR_X, $NR_{X.2}$ and OR_X wherein (each) R_X is selected from H, $C_{1\text{-}5}$alkyl, alkenyl;

ring heteroatom $X.b^3$ is selected from –S-, -O- and $–CH_2$-;

Rb^1 is selected from saturated or unsaturated, substituted or unsubstituted $C\text{-}_{1\text{-}4}$ aliphatic, or $C_{1\text{-}3}$ alicyclic optionally including one or more heteroatoms N, O, S, P, wherein substituent(s) are selected from one or more cycloalkyl, heterocyclic, hydroxy, oxo, halo, amine; preferably $R.b^1$ comprises a carbonyl substituted by H, alkyl or a linear or cyclic primary, secondary or tertiary amine, substituted $C_{1\text{-}3}$ alkyl, cycloalkyl or amide, more preferably cyclopropyl, or $CONHC_{1\text{-}3}$alkyl such as CONHEt or CH_2OH

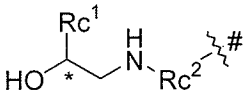
and each of $R.b^2$ and $R.b^3$ is selected from H, halo, hydroxy, thiol, amine, COOH, CHO, hydrazine, cyano or saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like, preferably from H, halo or hydroxy, preferably H or Cl;

Rb^4 is H;

-L.b- is as hereinbefore defined for –L-, more preferably saturated and unsaturated substituted or unsubstituted C_{1-12} aliphatic or C_{1-24} aromatic as defined for –L- preferably including one or more heteroatoms O, S or N, cyclic or heterocyclic groups, more preferably is of formula -L.I- or -L.II- as hereinbefore defined, most preferably is –(CH_2)m wherein m is 2 to 12, preferably 3, 4, 6 or 8, or is –(Ph-$CH_2CONH)_2$ $(CH_2)_2$-;

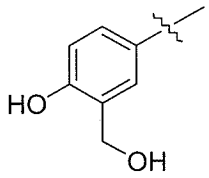
Lig.c is suitably a non-peptide of the formula

Lig.c $HOC^*(R.c^1)CH_2NH\text{-}R.c^2$-



Where * indicates an optically active centre and

Wherein R.c^1 is C_{6-14} aryl optionally including one or more heteroatoms selected from H, O, optionally substituted by OH, Hal eg Cl, NH_2, NHC_{1-3}alkyl, sulphonamide, oxoamine (-$CONH_2$) and the like, more preferably mono, di or tri substituted phenyl or quinoline wherein substituents include OH, Cl or NH_2, more preferably m-CH_2OH, p-OH phenyl, m-,p-dihydroxy phenol or m-,m-dihydroxyphenol, m-,m-diCl, p-NH_2 phenol, p-OH, m-$CONH_2$ phenol or 5-OH, 8-quinoline and the like, such as



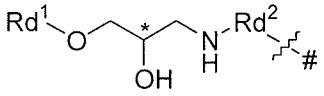
R.c^2 is selected from saturated or unsaturated, substituted or unsubstituted C_{1-20}, preferably C_{1-12}-, branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any optionally substituted C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like and combinations thereof;

Preferably R.c^2 is selected from C_{1-6} branched or straight chain aliphatic, C_{6-10} araliphatic optionally substituted by OH and optionally including heteroatoms selected from N,O, preferably including an ether O, such as selected from $-(CH_2)-{}_6OCH((CH_2)_3Ph)$, $CHCH_3(CH_2)_2Ph$, $CHCH_3CH_2PhOH$, $C(CH_3)_2CH_2$;

-L.c- is as hereinbefore defined for –L- and is suitably of formula -L.I- or -L.II- as hereinbefore defined, more preferably is selected from C_{1-12} alkyl, amide etc;

Lig.d is suitably a non-peptide of the formula

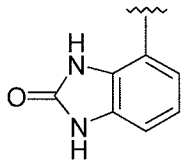
Lig.d R.d^1 $OCH_2C*HOHCH_2NH$-R.d^2-#

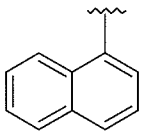


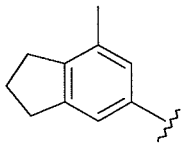
Where * indicates an optically active centre and where # indicates the site of linking to the fluorescent tagging moiety

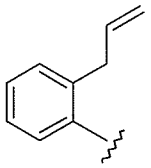
Wherein R.d^1 is saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like;

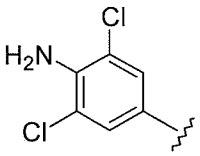
Preferably R.d[1] is substituted or unsubstituted C_{1-24} aralkyl or heteroaralkyl, including single ring and fused ring systems with (hetero)aryl or cycloalkyl rings, wherein optional substituents include C_{1-6} alkyl, alkoxy, ether, carbonyl, alkenyl, amine, amide each optionally carbonyl, amide, halo or OH subtitited, or halo such as chloro or OH, preferably R.d[1] is unsubstituted or substituted alkyl, alkenyl, halo, amine, amide, carbonyl, ketone, ether substituted phenyl or naphthyl, illustrated as follows, most preferably mono-, di-, tri- or tetra substituted mono or polycyclic fused aryl or cycloaryl or heterocycloaryl such as phenyl, carbazole or structures shown below or spiro ring systems, most preferably mono-, di-, tri- or tetra alkoxyalkyl, alkoxyalkoxyalkyl or CF_3 substituted phenyl or unsubstituted or monosubstituted naphthalene or 5,6 ring systems most preferably of the structures:





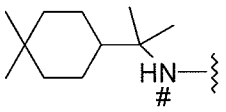


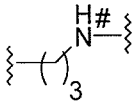




R.d[2] is substituted or unsubstituted amine, saturated or unsaturated, substituted or unsubstituted C_{1-12} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12}

aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like, more preferably amine, C_{1-6} branched or straight chain alkyl optionally including ether O, and optionally substituted by C_{6-10} aryl, for example of the formula:



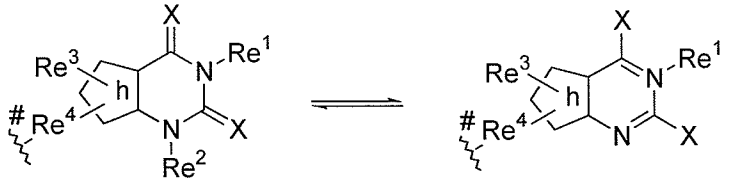


i.pr, i.bu, CH_2CH_2O (m-$CONH_2$, p-OH) phenol, CH_2CH_2O (o-OCH_3 phenol

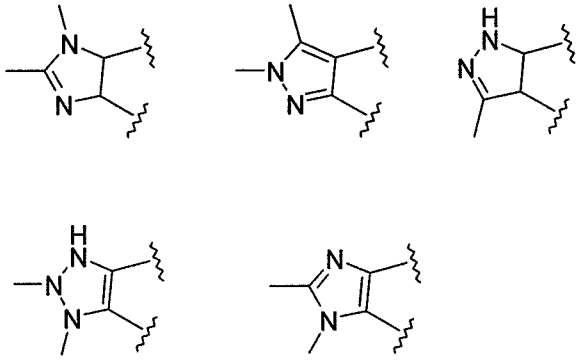
-L.d- is is as hereinbefore defined for –L- and is suitably of formula -L.I- or -L.II- as hereinbefore defined, more preferably is ~~a single bond or is~~ as hereinbefore defined for -L.a-;

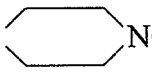
Lig.e comprises a cell permeant moiety or is associated with a cell permeant L or Fl moiety and is suitably of the formula , in either of the following forms given:

Lig.e[1]



wherein h is selected from



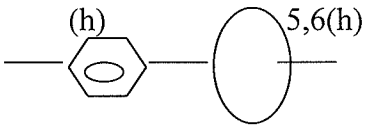
each optionally substituted by R.e^3 – R.e^4 wherein R.e^1 – R.e^4 are as R.a^1 – R.a^4 defined above or in which R.e^3 is $C_{5\text{-}9}$linear or branched alkyl, optionally mono or multi hydroxy or halo substituted or is aryl optionally substituted by alkoxy, sulfonyl and the like eg ortho-OEt, meta-SO_2N  NCH_3

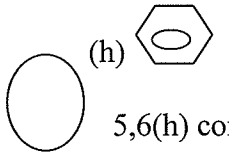
each X is independently selected from H, =O, -OR.e^2, =N, HN, NR.e^5, HR.e^6 , and aryl optionally substituted by ether; or X is aryl optionally alkyl or alkoxy substituted such as Ph-ortho-$OCH_2CH_2CH_3$;

and where R.e^5 is as defined above for R.e^1 above or forms a fused cyclic ring together with the adjacent ring N atom; preferably 1 or 2 fused 5 membered cyclic rings;

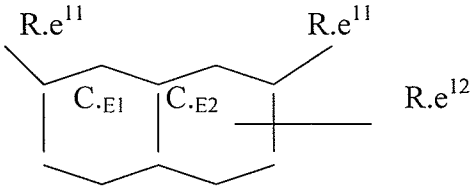
and R.e^6 is as defined above for R.e^1 above or is selected from optionally substituted phenyl wherein optional substituents include ether such as o-ethoxy or o-propoxy, alkyl, OH and the like, sulphonyl, carbonyl and the like substituted by heterocyclic, or cyclic $C_{5\text{-}8}$ alkyl such as methyl, piperazinyl, sulphonyl and the like;

or Lig.e is of the formula Lig.e^2

Lig.e^2 

Wherein each spiro ring optionally comprises zero or one or more heteroatoms h which are preferably N, more preferably  comprises zero or 1 N heteroatom and 5,6(h) comprises zero, 1 or 2 N heteroatoms and is unsaturated or comprises one or two –C=C- or -C=N- groups; and wherein each ring is optionally substituted by one or more oxo, CO, COOH, C_{1-6} alkyl or linear or cyclic alkoxy such as methoxy, ethoxy or cyclopentyloxy optionally substituted by one or more oxo, CO, COOH, CN, or C_{1-6} alicyclic or amine groups, amine or one or more spiro or fused heterocycles;

or Lig.e is of the formula Lig.e^3

Lig.e^3 

Wherein each of $C._{E1}$ and $C._{E2}$ is independently selected from aryl, heteroaryl, cyloalkyl and heterocyclic, more preferably from phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring –C=C- group;

Each of up to seven $R.e^{11}$ is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}20}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from any $C_{1\text{-}12}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like, such as =O, OCH_3, $CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

or any two or more of $R.e^{11}$ form a one, two or three ring fused cyclic structure, preferably comprising a fused 3 ring aryl, 5-heterocyclic, 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic $Lig.e^3$ structure;

and $R.e^{12}$ is a moiety as defined for $R.e^{11}$ above;

Preferably Lig.e is of the formula $Lig.e^1$ as hereinbefore defined in particular

where $R.e^2$ and $R.e^3$ are respectively propyl and butyl;

-L.e- is suitably as hereinbefore defined for -L.a-.

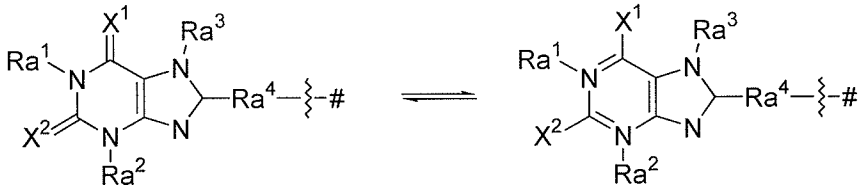
94. (Withdrawn-Previously Presented) Library as claimed in claim 93 wherein the or each Fl is selected from the following dyes: Texas red™, coumarin and derivatives, Cascade Blue™, EvoBlue and fluorescent derivatives thereof, pyrenes and pyridyloxazole derivatives, the cyanine dyes, the dyomics (DY dyes and ATTO dyes) and fluorescent derivatives thereof, the Alexafluor dyes and derivatives, BDI dyes including the commercially available Bodipy™ dyes,

pyrenes, anthracenes, acridines, fluorescent phycobiliproteins and their conjugates and fluoresceinated microbeads, and Texas Red derivatives, coupled to amine groups using the isocyanate, succinimidyl ester or dichlorotriazinyl-reactive groups.

95. (Withdrawn-Currently Amended) Compound which is a tagged non-peptide ligand comprising moiety Lig and L selected from formula Lig.a-L.a- - Lig.e-L.e associated with a Tag which is an entity –Fl wherein –Fl is selected from a red, near ir or blue dye and wherein and the compound comprises pharmacological activity as a fluorescent GPCR ligand agonist or fluorescent GPCR ligand antagonist ~~o~~for GPCR receptor binding and activation or inhibition.

Lig.a- is suitably of the formula, in either of the following forms given:

Lig.a [1]-



Wherein X^1 and X^2 are each independently selected from H, =O, OR.a, NR.a, NHR.a;

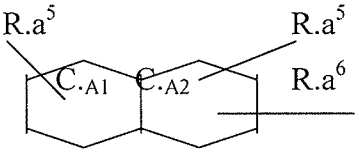
X^1 and X^2 are each preferably =O;

each of R.a, R.a^1, R.a^2 and R.a^3 independently is selected from H or C_{1-4} linear or branched alkyl, preferably H, methyl, ethyl, n-propyl, isopropyl, n-butyl, t-butyl or isobutyl optionally mono or multi hydroxy or halo substituted, such as CH_2OH, CH_2F or $CH_2CHOHCH_2OH$;

$R.a^4$ is selected from a heteroatom O, S or substituted or unsubstituted amine or saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like;

preferably $R.a^4$ is selected from optionally substituted aryl, cycloalkyl, alkyl, ketone, (di)amine, (di)amide, more preferably optionally substituted alkoxy, cycloalkyl, amine, amide, carboxylic acid or optionally o-, m- or p- substituted phenyl wherein substituents include aryl, alkyl, cycloalkyl, heteroaryl or heteroalkyl, amine, amide, carboxyl, carbonyl etc, for example is cyclohexyl, cyclopentyl, ethoxy, $(CH_2)_2PhPh$, CH_2Ph, $CONH(CH_2)nCONH$, $CH_2CONH(CH_2)_2NH$, $CH_2PhNHCOCH_2$, $CH_2CH_2OCOCH_2$, succinimidyl ester, $NHCOCH_2$, $CH_2(CH_3)NCOCH_2$, $H_2N(CH_2)_2NHCOCH_2$, $H_2N(CH_2)_8NHCOCH_2$, $H_2NNHCOCH_2$, $CH_2CONH(CH_2)_2NHCOCH_2$, $HOPhCH_2N(CH_2CH_3.HOAc)(CH_2)_2NHCOCH_2$, heterocyclic-$(CH_2)_4CONH(CH_2)_2NHCOCH_2$, heterocyclic-$NHCON(heterocyclic)COCH_2$ and the like;

or Lig.a- is of the formula Lig.a^2-

Lig.a^2 

wherein each of $C._{A1}$ and $C._{A2}$ is independently selected from aryl, heteroaryl, cyloalkyl and heterocyclic, more preferably from phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring -C=C- group;

Each of up to seven R.a^5 is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from H, halo, hydroxy, thiol, amine, COOH, hydrazine, cyano, saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}20}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from any $C_{1\text{-}12}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like, such as =O, OCH_3, $CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

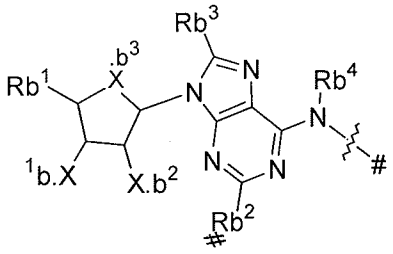
or any two or more of R.a^5 form a one, two or three ring fused cyclic structure, preferably comprising a fused 3 ring aryl, 5-heterocyclic, 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic Lig.a^2structure;

and R.a^6 is a moiety as defined for R.a^5 above;

and -L.a- is as hereinbefore defined for -L- and is suitably of formula -L.I- or -L.II- as hereinbefore defined, more preferably is selected from ~~a single bond,~~ amino acid or amide such as a peptide or polypeptide for example gly or gly_3, alkyl of formula $-(CH_2)_n$ where n is 3 to 8, preferably 3, 4 or 6, optionally including one or more heteroatoms or unsaturated groups, such as –O- or –S- or –CH=CH- and the like:

Lig.b is suitably of the formula Lig.b

Lig.b



wherein ring substituents $X.b^1$ and $X.b^2$ are independently selected from hydrocarbon such as alkyl or SR_X, $NR_{X.2}$ and OR_X wherein (each) R_X is selected from H, C_{1-5}alkyl, alkenyl;

ring heteroatom $X.b^3$ is selected from –S-, -O- and $-CH_2-$;

Rb^1 is selected from saturated or unsaturated, substituted or unsubstituted C_{-1-4} aliphatic, or C_{1-3} alicyclic optionally including one or more heteroatoms N, O, S,

P, wherein substituent(s) are selected from one or more cycloalkyl, heterocyclic, hydroxy, oxo, halo, amine; preferably $R.b^1$ comprises a carbonyl substituted by H, alkyl or a linear or cyclic primary, secondary or tertiary amine, substituted C_{1-3} alkyl, cycloalkyl or amide, more preferably cyclopropyl, or $CONHC_{1-3}$alkyl such as CONHEt or CH_2OH

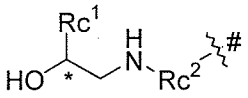
and each of $R.b^2$ and $R.b^3$ is selected from H, halo, hydroxy, thiol, amine, COOH, CHO, hydrazine, cyano or saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like, preferably from H, halo or hydroxy, preferably H or Cl;

Rb^4 is H;

-L.b- is as hereinbefore defined for –L-, more preferably saturated and unsaturated substituted or unsubstituted C_{1-12} aliphatic or C_{1-24} aromatic as defined for –L- preferably including one or more heteroatoms O, S or N, cyclic or heterocyclic groups, more preferably is of formula -L.I- or -L.II- as hereinbefore defined, most preferably is –(CH_2)m wherein m is 2 to 12, preferably 3, 4, 6 or 8, or is –(Ph-$CH_2CONH)_2$ $(CH_2)_2$-;

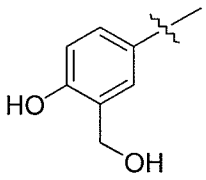
Lig.c is suitably a non-peptide of the formula

Lig.c $HOC^*(R.c^1)CH_2NH\text{-}R.c^2\text{-}$



Where * indicates an optically active centre and

Wherein $R.c^1$ is $C_{6\text{-}14}$ aryl optionally including one or more heteroatoms selected from H, O, optionally substituted by OH, Hal eg Cl, NH_2, $NHC_{1\text{-}3}$alkyl, sulphonamide, oxoamine ($-CONH_2$) and the like, more preferably mono, di or tri substituted phenyl or quinoline wherein substituents include OH, Cl or NH_2, more preferably m-CH_2OH, p-OH phenyl, m-,p-dihydroxy phenol or m-,m-dihydroxyphenol, m-,m-diCl, p-NH_2 phenol, p-OH, m-$CONH_2$ phenol or 5-OH, 8-quinoline and the like, such as



$R.c^2$ is selected from saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}20}$, preferably $C_{1\text{-}12}$-, branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms

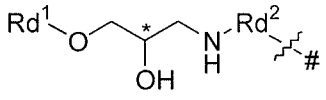
selected from N, O, S, P; wherein optional substituents are selected from any optionally substituted C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like and combinations thereof;

Preferably $R.c^2$ is selected from C_{1-6} branched or straight chain aliphatic, C_{6-10} araliphatic optionally substituted by OH and optionally including heteroatoms selected from N,O, preferably including an ether O, such as selected from $-(CH_2)-{}_6OCH((CH_2)_3Ph)$, $CHCH_3(CH_2)_2Ph$, $CHCH_3CH_2PhOH$, $C(CH_3)_2CH_2$;

-L.c- is as hereinbefore defined for –L- and is suitably of formula -L.I- or -L.II- as hereinbefore defined, more preferably is selected from C_{1-12} alkyl, amide etc;

Lig.d is suitably a non-peptide of the formula

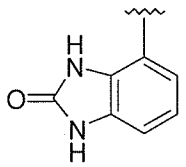
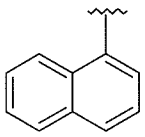
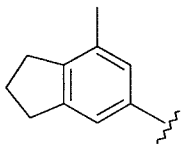
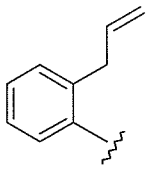
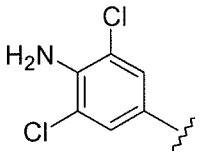
Lig.d $R.d^1\ OCH_2C^*HOHCH_2NH\text{-}R.d^2\text{-}\#$



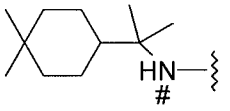
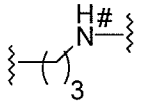
Where * indicates an optically active centre and where # indicates the site of linking to the fluorescent tagging moiety

Wherein $R.d^1$ is saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like;

Preferably $R.d^1$ is substituted or unsubstituted C_{1-24} aralkyl or heteroaralkyl, including single ring and fused ring systems with (hetero)aryl or cycloalkyl rings, wherein optional substituents include C_{1-6} alkyl, alkoxy, ether, carbonyl, alkenyl, amine, amide each optionally carbonyl, amide, halo or OH subtitited, or halo such as chloro or OH, preferably $R.d^1$ is unsubstituted or substituted alkyl, alkenyl, halo, amine, amide, carbonyl, ketone, ether substituted phenyl or naphthyl, illustrated as follows, most preferably mono-, di-, tri- or tetra substituted mono or polycyclic fused aryl or cycloaryl or heterocycloaryl such as phenyl, carbazole or structures shown below or spiro ring systems, most preferably mono-, di-, tri- or tetra alkoxyalkyl, alkoxyalkoxyalkyl or CF_3 substituted phenyl or unsubstituted or monosubstituted naphthalene or 5,6 ring systems most preferably of the structures:

R.d^2 is substituted or unsubstituted amine, saturated or unsaturated, substituted or unsubstituted C_{1-12} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like, more preferably amine, C_{1-6} branched or straight chain alkyl optionally including ether O, and optionally substituted by C_{6-10} aryl, for example of the formula:

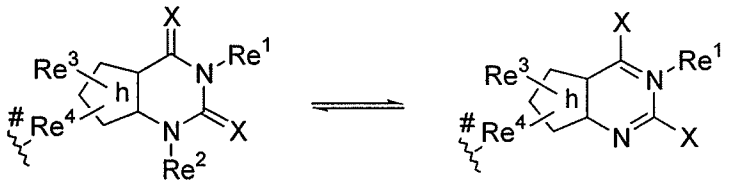



i.pr, i.bu, CH_2CH_2O (m-$CONH_2$, p-OH) phenol, CH_2CH_2O (o-OCH_3 phenol

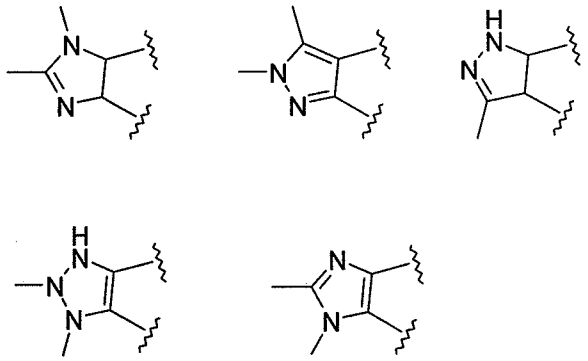
-L.d- is is as hereinbefore defined for –L- and is suitably of formula -L.I- or -L.II- as hereinbefore defined, more preferably is ~~a single bond or is~~ as hereinbefore defined for -L.a-;

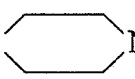
Lig.e comprises a cell permeant moiety or is associated with a cell permeant L or Fl moiety and is suitably of the formula , in either of the following forms given:

Lig.e[1]



wherein h is selected from



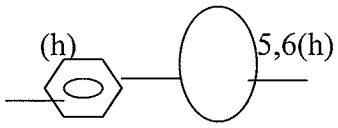
each optionally substituted by R.e[3] – R.e[4] wherein R.e[1] – R.e[4] are as R.a[1] – R.a[4] defined above or in which R.e[3] is $C_{5\text{-}9}$linear or branched alkyl, optionally mono or multi hydroxy or halo substituted or is aryl optionally substituted by alkoxy, sulfonyl and the like eg ortho-OEt, meta-SO_2N  NCH_3

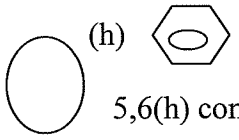
each X is independently selected from H, =O, -OR.e^2, =N, HN, NR.e^5, HR.e^6 , and aryl optionally substituted by ether; or X is aryl optionally alkyl or alkoxy substituted such as Ph-ortho-$OCH_2CH_2CH_3$;

and where R.e^5 is as defined above for R.e^1 above or forms a fused cyclic ring together with the adjacent ring N atom; preferably 1 or 2 fused 5 membered cyclic rings;

and R.e^6 is as defined above for R.e^1 above or is selected from optionally substituted phenyl wherein optional substituents include ether such as o-ethoxy or o-propoxy, alkyl, OH and the like, sulphonyl, carbonyl and the like substituted by heterocyclic, or cyclic C_{5-8} alkyl such as methyl, piperazinyl, sulphonyl and the like;

or Lig.e is of the formula Lig.e^2

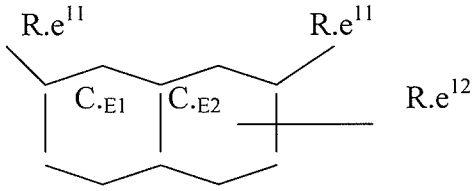
Lig.e^2 

Wherein each spiro ring optionally comprises zero or one or more heteroatoms h which are preferably N, more preferably 

comprises zero or 1 N heteroatom and 5,6(h) comprises zero, 1 or 2 N

heteroatoms and is unsaturated or comprises one or two –C=C- or -C=N- groups; and wherein each ring is optionally substituted by one or more oxo, CO, COOH, C_{1-6} alkyl or linear or cyclic alkoxy such as methoxy, ethoxy or cyclopentyloxy optionally substituted by one or more oxo, CO, COOH, CN, or C_{1-6} alicyclic or amine groups, amine or one or more spiro or fused heterocycles;

or Lig.e is of the formula $Lig.e^3$

$Lig.e^3$ 

Wherein each of $C._{E1}$ and $C._{E2}$ is independently selected from aryl, heteroaryl, cyloalkyl and heterocyclic, more preferably from phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring –C=C- group;

Each of up to seven $R.e^{11}$ is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore

defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano, and the like, such as =O, OCH_3, $CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

or any two or more of $R.e^{11}$ form a one, two or three ring fused cyclic structure, preferably comprising a fused 3 ring aryl, 5-heterocyclic, 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic $Lig.e^3$ structure;

and $R.e^{12}$ is a moiety as defined for $R.e^{11}$ above;

Preferably Lig.e is of the formula $Lig.e^1$ as hereinbefore defined in particular where $R.e^2$ and $R.e^3$ are respectively propyl and butyl;

-L.e- is suitably as hereinbefore defined for -L.a-.

96. (Withdrawn-Previously Presented) Compound as claimed in claim 95 wherein Fl is selected from the following dyes: Texas red™, coumarin and derivatives, Cascade Blue™, EvoBlue and fluorescent derivatives thereof, pyrenes and pyridyloxazole derivatives, the cyanine dyes, the dyomics (DY dyes and ATTO dyes) and fluorescent derivatives thereof, the Alexafluor dyes and derivatives, BDI dyes including the commercially available Bodipy™ dyes, pyrenes, anthracenes, acridines, fluorescent phycobiliproteins and their conjugates and fluoresceinated microbeads, and Texas Red derivatives, coupled to amine groups using the isocyanate, succinimidyl ester or dichlorotriazinyl-reactive groups.

97. (Withdrawn-Previously Presented) Process for the preparation of a library as claimed in Claim 59, wherein reactive groups Y_{Lig}, Y_L, Y_T have suitable reactive group functionalities for linking by addition or addition – elimination reaction.

98. (Withdrawn-Previously Presented) Process for the preparation of a compound as claimed in Claim 60, wherein reactive groups Y_{Lig}, Y_L, Y_T have suitable reactive group functionalities for linking by addition or addition – elimination reaction.

99. (Withdrawn and Currently Amended) Compound as claimed in Claim ~~47~~ 64 wherein ~~a GPCR ligand~~Lig is a ligand selected from any compound which is effective as an agonist or antagonist for an adenosine receptor, a beta-adrenoceptor, a muscarinic receptor, a histamine receptor, an opiate receptor, a cannabinoid receptor, a chemokine receptor, an alpha-adrenoceptor, a GABA receptor, a prostanoid receptor, a 5-HT (serotonin) receptor, an excitatory aminoacid receptor (glutamate), a dopamine receptor, a protease-activating receptor, a neurokinin receptor, an angiotensin receptor, an oxytocin receptor, a leukotriene receptor, a nucleotide receptor (purines and pyrimidines), a calcium-sensing receptor, a thyroid-stimulating hormone receptor, a neurotensin receptor, a vasopressin receptor, an olfactory receptor, a nucleobase receptor (adenosine), a lysophosphatidic acid receptor, a sphingolipid receptor, a tyramine receptor (trace amines), a free-fatty acid receptor and a cyclic nucleotide receptor~~;~~ ~~an inhibitor of intracellular enzymes is an inhibitor of cyclic nucleotide phosphodiesterases; and a substrate or inhibitor of a drug transporter is selected from a substrate or inhibitor of an equilibrium based drug transporter or ATP driven pump selected from a catecholamine~~

~~transporter, a nucleoside transporter, an ATP-binding cassette transporter, a cyclic nucleotide transporter or derivatives or analogues thereof~~ ;

or wherein Lig is selected from

a) xanthine like structures including XAC, theophylline, caffeine, theobromine, dyphilline, enprofylline; or fused biaryl structures including papaverine, dihydroquinilones, cilostamide, dipyridamole or vinpocetine; and analogues thereof;

b) adenosine like structures including ADAC, NECA and analogues thereof;

c) ethanolamine like structures including salmeterol, salbutamol, terbutaline, quinprenaline, labetalol, sotalol, bambuterol, fenoterol, reprotolol, tulobuterol, clenbuterol and analogues thereof;

d) oxypropanolamine like structures including CGP12177, propranolol, practolol, acebutalol, betaxolol, ICI 118551, alprenolol, celiprolol (celectol), metoprolol (betaloc), CGP20712A, atenolol, bisoprolol, misaprolol, carvedilol, bucindolol, esmolol, nadolol, nebivolol, oxprenolol, xamoterol, pindolol, timolol and analogues thereof;

e) xanthine like structures including XAC, theophylline, caffeine, theobromine, dyphilline, enprofylline, sildenafil, EHNA (erythro-9-(2-hydroxyl-3-nonyl)adenine), zaprinast; or spiro bicyclic structures including bypyridines, amrinone; imidazolines, CI930; dihydropyridazinones, indolan, rolipram, SB207499; or fused biaryl structures including papaverine, dihydroquinilones, cilostamide, dipyridamole, vinpocetine and analogues thereof.

100. (Withdrawn-Currently Amended) Compound as claimed in Claim ~~47~~ 64 wherein each compound of formula I or I' comprises a moiety Lig and L as hereinbelow defined:

Wherein:

any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers

$Lig.a_m$ is suitably of the formula, in either of the following forms given, including any of its

possible linking configurations or sites:

$Lig.a^1{}_m$

Wherein at least one or all of Ra^1 to Ra^4, X^1 and X^2 comprise a linking site or functionality J as hereinbefore defined

X^1 and X^2 are each independently selected from H, O, OR.a, NR.a, NHR.a;

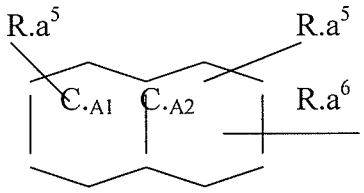
X^1 and X^2 are each preferably O;

each of $R.a^1$, $R.a^2$, $R.a^3$ and $R.a^4$ independently is selected from H or C_{1-4} linear or branched alkyl optionally mono or multi hydroxy or halo substituted;

$R.a^4$ is selected from a heteroatom O, S or substituted or unsubstituted amine or saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo and cyano;

including optionally substituted aryl, cycloalkyl, alkyl, ketone, (di)amine, (di)amide, alkoxy, cycloalkyl, carboxylic acid or optionally o-, m- or p-substituted phenyl wherein substituents include aryl, alkyl, cycloalkyl, heteroaryl or heteroalkyl, amine, amide, carboxyl, carbonyl or $R.a^4$ comprises cyclohexyl, cyclopentyl, ethoxy, $(CH_2)_2PhPh$, CH_2Ph, $CONH(CH_2)nCONH$, $CH_2CONH(CH_2)_2NH$, $CH_2PhNHCOCH_2$, $CH_2CH_2OCOCH_2$, succinimidyl ester, $NHCOCH_2$, $CH_2(CH_3)NCOCH_2$, $H_2N(CH_2)_2NHCOCH_2$, $H_2N(CH_2)_8NHCOCH_2$, $H_2NNHCOCH_2$, $CH_2CONH(CH_2)_2NHCOCH_2$, $HOPhCH_2N(CH_2CH_3.HOAc)(CH_2)_2NHCOCH_2$, heterocyclic-$(CH_2)_4CONH(CH_2)_2NHCOCH_2$ or heterocyclic-$NHCON(heterocyclic)COCH_2$;

or Lig.a is of the formula Lig.a^2-

Lig.a^2 

wherein at least one or all of Ra^5 to Ra^6, or a cyclic C or heteroatom comprise a linking site or functionality J as hereinbefore defined,

each of $C._{A1}$ and $C._{A2}$ is independently selected from C_{5-6} aryl, heteroaryl, cycloalkyl and heterocyclic, more preferably from phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring –C=C- group;

Each of up to seven R.a^5 is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from H, halo, hydroxy, thiol, amine, COOH, hydrazine, cyano, saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo =O or cyano; OCH_3, $CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

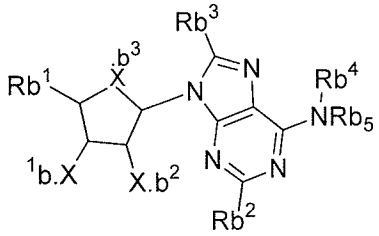
or any two or more of R.a^5 form a one, two or three ring fused cyclic structure, a fused 3 ring aryl, 5-heterocyclic or 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic Lig.a^2structure;

and R.a^6 is a moiety as defined for R.a^5 above;

and L.a is as hereinbefore defined for L or J_L L J_T or L.I or subformulae as hereinbefore defined, or is ~~a single bond,~~ amino acid or amide including a peptide or polypeptide gly or gly_3, alkyl of formula $-(CH_2)_n$ where n is 3 to 8, optionally including one or more heteroatoms or unsaturated groups, including –O- or –S- or –CH=CH-:

Lig.b is suitably of the formula Lig.b including any of its possible linking configurations or sites:

Lig.b



wherein at least one or all of Rb^1 to Rb^5 or Xb^1 to Xb^3 comprise a linking site or functionality J as hereinbefore defined

ring substituents $X.b^1$ and $X.b^2$ are independently selected from hydrocarbon including alkyl or SR_X, $NR_{X.2}$ and OR_X wherein (each) R_X is selected from H, $C_{1\text{-}5}$alkyl, alkenyl;

ring heteroatom $X.b^3$ is selected from –S-, -O- and $-CH_2$-;

Rb^1 is selected from saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}4}$ aliphatic, or $C_{1\text{-}3}$ alicyclic optionally including one or more heteroatoms N, O, S, P, wherein substituent(s) are selected from one or more cycloalkyl, heterocyclic, hydroxy, oxo, halo, amine; or $R.b^1$ comprises a carbonyl substituted by H, alkyl or a linear or cyclic primary, secondary or tertiary amine, substituted $C_{1\text{-}3}$ alkyl,

cycloalkyl or amide, cyclopropyl, or $CONHC_{1-3}$alkyl including CONHEt or CH_2OH

and each of $R.b^2$ and $R.b^3$ is selected from H, halo, hydroxy, thiol, amine, COOH, CHO, hydrazine, cyano or saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano, preferably from H, halo or hydroxy;

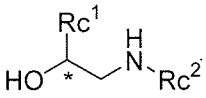
Rb^4 is H;

Rb^5 is H or alkyl

L.b comprises a linking site or functionality J as hereinbefore defined; and is as hereinbefore defined for L or its subformulae, more preferably is saturated and unsaturated substituted or unsubstituted C_{1-12} aliphatic or C_{1-24} aromatic as defined for L optionally including one or more heteroatoms O, S or N, cyclic or heterocyclic groups, or is of formula L.I or its subformulae as hereinbefore defined, or is (CH_2)m wherein m is 2 to 12, or is (Ph-$CH_2CONH)_2$ $(CH_2)_2$;

Lig.c is of the formula Lig.c including any of its possible linking configurations or sites:

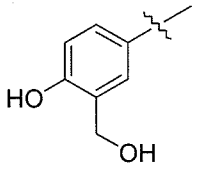
Lig.c $HOC^*(R.c^1)CH_2NH\text{-}R.c^2$



where at least one or all of Rc^1 to Rc^2 or OH, or a chain C or N comprise a linking site or functionality J as hereinbefore defined

* indicates an optically active centre and

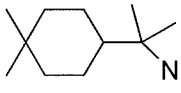
wherein $R.c^1$ is $C_{6\text{-}14}$ aryl optionally including one or more heteroatoms selected from H, O, optionally substituted by OH, Hal, NH_2, $NHC_{1\text{-}3}$alkyl, sulphonamide, oxoamine or ($-CONH_2$), or is mono, di or tri substituted phenyl or quinoline wherein substituents include OH, Cl or NH_2, or is m-CH_2OH, p-OH phenyl, m-,p-dihydroxy phenol or m-,m-dihydroxyphenol, m-,m-diCl, p-NH_2 phenol, p-OH, m-$CONH_2$ phenol or 5-OH, 8-quinoline,

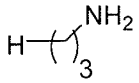


$R.c^2$ is selected from saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}20}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any optionally substituted $C_{1\text{-}12}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or

more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano and combinations thereof;

or R.c^2 is selected from C_{1-6} branched or straight chain aliphatic, C_{6-10} araliphatic optionally substituted by OH and optionally including heteroatoms selected from N,O, optionally including an ether O, and is selected from $-(CH_2)-{}_6OCH((CH_2)_3Ph)$, $CHCH_3(CH_2)_2Ph$, $CHCH_3CH_2PhOH$, $C(CH_3)_2CH_2Ph$ or from the structures:

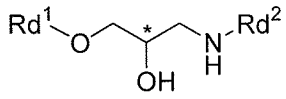




L.c is present as R.c^2 or comprises a linking site or functionality J as hereinbefore defined, and is as hereinbefore defined for L, formula L.I or its subformulae as hereinbefore defined, or is selected from C_{1-12} alkyl, amide;

Lig.d is of the formula Lig.d including any of its possible linking configurations or sites:

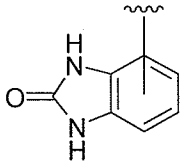
Lig.d R.d^1 $OCH_2C*HOHCH_2NH$-R.d^2

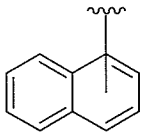


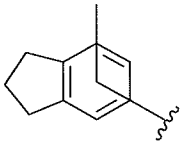
where at least one or all of Rd^1 to Rd^2 or OH, a chain C or N comprise a linking site or functionality J as hereinbefore defined

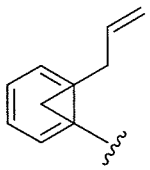
* indicates an optically active centre

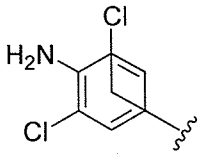
wherein $R.d^1$ is saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano; or $R.d^1$ is substituted or unsubstituted C_{1-24} aralkyl or heteroaralkyl, including single ring and fused ring systems with (hetero)aryl or cycloalkyl rings, wherein optional substituents include C_{1-6} alkyl, alkoxy, ether, carbonyl, alkenyl, amine, amide each optionally carbonyl, amide, halo or OH substituted, or halo or OH, amine, amide, carbonyl, ketone, ether substituted phenyl or naphthyl, mono-, di-, tri- or tetra substituted mono or polycyclic fused aryl or cycloaryl or heterocycloaryl including phenyl, carbazole or structures shown below or spiro ring systems, mono-, di-, tri- or tetra alkoxyalkyl, alkoxyalkoxyalkyl or CF_3 substituted phenyl or unsubstituted or monosubstituted naphthalene or 5,6 ring systems:



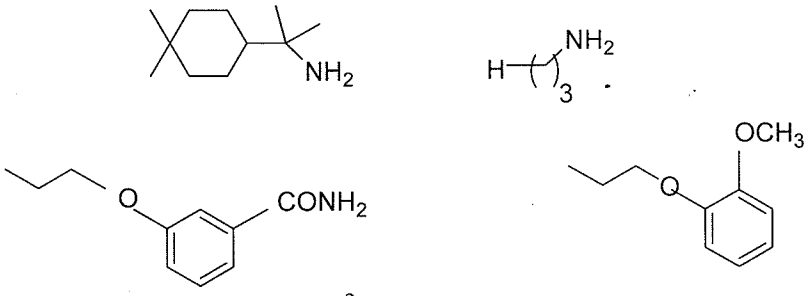








R.d^2 is substituted or unsubstituted amine, saturated or unsaturated, substituted or unsubstituted C_{1-12} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano, more preferably amine, C_{1-6} branched or straight chain alkyl optionally including ether O, and optionally substituted by C_{6-10} aryl, or of the formula:



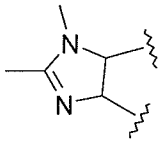
L.d may be present as R.d^2 or may comprise a linking site or functionality J as hereinbefore defined and is as hereinbefore defined for L and its subformulae , formula L.I and its subformulae as hereinbefore defined, or is ~~a single bond or~~ is as hereinbefore defined for L.a;

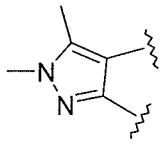
Lig.e comprises a cell permeant moiety or is associated with a cell permeant L or Fl moiety or is of the formula , in either of the following forms given including any of its possible linking configurations or sites:

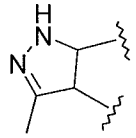
Lig.e[1]

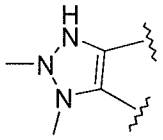
wherein at least one or all of Re^1 to Re^4, X and a ring C or N comprise a linking site or functionality J as hereinbefore defined

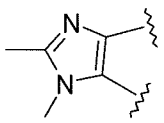
h is selected from



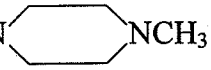








each optionally substituted by $R.e^3$ – $R.e^4$ wherein $R.e^1$ – $R.e^4$ are as $R.a^1$ – $R.a^4$ defined above or in which $R.e^3$ is C_{5-9} linear or branched alkyl, optionally mono or multi hydroxy or halo substituted or is aryl optionally substituted by alkoxy or sulfonyl,

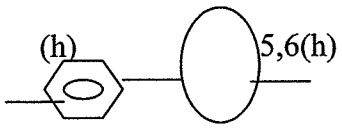
ortho-OEt, meta- 

each X is independently selected from H, O, -OR.e^2, N, HN, NR.e^5, HR.e^6 , and aryl optionally substituted by ether; or X is aryl optionally alkyl or alkoxy substituted or is Ph-ortho-$OCH_2CH_2CH_3$;

and where R.e^5 is as defined above for R.e^1 above or forms a fused cyclic ring together with the adjacent ring N atom, or 1 or 2 fused 5 membered cyclic rings;

and R.e^6 is as defined above for R.e^1 above or is selected from optionally substituted phenyl wherein optional substituents include ether, o-ethoxy or o-propoxy, alkyl or OH, sulphonyl or carbonyl substituted by heterocyclic, or cyclic C_{5-8} alkyl, piperazinyl or sulphonyl;

or Lig.e is of the formula Lig.e^2

Lig.e^2 

wherein at least one or all free ring atom or their substituents comprise a linking site or functionality J as hereinbefore defined

each spiro ring optionally comprises zero or one or more heteroatoms h

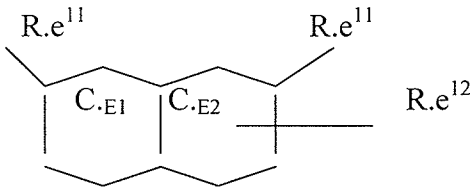
or (h)  comprises zero or 1 N heteroatom and

5,6(h)  comprises

zero, 1 or 2 N heteroatoms and is unsaturated or comprises one or two –C=C- or -C=N- groups;

and wherein each ring is optionally substituted by one or more oxo, CO, COOH, C_{1-6} alkyl or linear or cyclic alkoxy optionally substituted by one or more oxo, CO, COOH, CN, or C_{1-6} alicyclic or amine groups, amine or one or more spiro or fused heterocycles;

or Lig.e is of the formula $Lig.e^3$

$Lig.e^3$ 

wherein at least one or all of Re^{11} to Re^{12}, or a ring C or heteroatom or ring substituent comprise a linking site or functionality J as hereinbefore defined

each of $C._{E1}$ and $C._{E2}$ is independently selected from C_{5-6} aryl, heteroaryl, cyloalkyl and heterocyclic, including phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring –C=C- group;

each of up to seven R.e^{11} is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo =O, or cyano, OCH_3, $CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

or any two or more of R.e^{11} form a one, two or three ring fused cyclic structure, a fused 3 ring aryl, 5-heterocyclic or 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic Lig.e^3 structure;

and R.e^{12} is a moiety as defined for R.e^{11} above;

L.e comprises a linking site or functionality J as hereinbefore defined and is suitably as hereinbefore defined for L.a.

101. (New) The compound of Claim 64 wherein Lig and the compound of formula I or I' are selected from a GPCR ligand agonist or activator of GPCR receptor binding or functionality and a GPCR ligand antagonist or inhibitor of receptor binding or functionality.

102. (New) The compound of Claim 64 which is an agonist which maintains its binding affinity and functional activity or is an antagonist which maintains its binding affinity on linking or when linked to fluorescent moiety Fl.

103. (New) The compound of Claim 64 which has affinity such that it binds semi-permanently or transiently and remains bound when unbound ligand is washed away.

104. (New) The compound of Claim 64 wherein L is selected from a short, medium or long chain moiety and prevents loss of affinity of ligand by distancing the Fl moiety from the Lig moiety, preventing interference with GPCR receptor binding.

105. (New) The compound of Claim 64 wherein J_{Lm} L J_{Tm} comprises a polypeptide, peptide or polyether

106. (New) The compound of formula I

$(Lig\ J_L)_m\ L(J_TTag)_m(J_TL(J_LLig)_m)_p$

or salt thereof

comprising ligand moiety Lig linked to tag moiety Tag via linker moiety L at linking site or linking functionality J_T and J_L

wherein Lig is a ligand selected from a non-peptide GPCR ligand agonist and a non-peptide GPCR ligand antagonist, wherein the Lig comprises pharmacological activity as an agonist or antagonist for GPCR receptor binding and activation or inhibition,

L is selected from is selected from amine, amide, and saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}600}$ branched or straight chain aliphatic, aromatic,

alicyclic and combinations thereof which comprise one or more heteroatoms selected from N, O, and optionally additionally S, P, wherein optional substituents are selected from any C_{1-20} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano and carbonyl and combinations thereof;

m are each independently selected from a whole number integer from 1 to 3;

p is 0 to 3

wherein -Tag is a fluorophore entity -Fl, whereby the compound is of formula I'

$(LigJ_L)_m$ L $(J_T\ Fl)_m$ $(J_T$ L $(J_L Lig)_m)_p$

and the compound of formula I retains pharmacological activity as a fluorescent GPCR ligand agonist or fluorescent GPCR ligand antagonist for GPCR receptor binding and activation or inhibition,

wherein L is oligomeric having oligomeric repeat of 2 to 30 or polymeric having polymeric repeat in excess of 30 up to 300

with the proviso that:

when Lig is XAC ie in Lig.a when each of $R.a^1$ and $R.a^2$ is propyl, $R.a^3$ is H and $R.a^4$ is –Ph-$OCH_2CONH(CH_2)_2NH$-, and L is gly3, Fl is not fluorescein;

when Lig is ADAC , ie $R.b^1$ is CH_2OH, $R.b^2$ and $R.b^3$ are H and L is –(Ph-$CH_2CONH)_2(CH_2)_2$-, Fl is not fluorescein, NBD or Rhodamine.

107. (New) The compound of Claim 106 wherein L is selected from a short, medium or long chain moiety and prevents loss of affinity of ligand by distancing the Fl moiety from the Lig moiety, preventing interference with GPCR receptor binding.

108. (New) The compound of Claim 106 wherein J_{Lm} L J_{Tm} comprises a polypeptide, peptide or polyether.

109. (New) The compound of Claim 64, having verified pharmacology for binding to or inhibition of a GPCR receptor including measure of affinity or inhibition.

110. (New) The compound of Claim 64 having verified pharmacological properties defined in terms of cells expressing a GPCR receptor as hereinbefore defined and given as the Inhibition or Antagonism of receptor binding or of receptor functionality together with a value for the Inhibition (pK_B) or Antagonism (pK_I) binding constants, and optionally together with fluorescent images of the pharmacological binding in single living cells illustrating the defined inhibition or antagonism, which are determined by virtue of its Spectral Properties including Excitation Max and Emission Max, Fluorescence Lifetime and Emission quantum yield.

111. (New) The compound of Claim 64 having verified pharmacological properties defined in terms of EC_{50} values for agonist stimulated – or pK_i values for antagonism of agonist stimulated second messenger generation.

112. (New) The compound of Claim 111 wherein pharmacology is defined in terms of a cell or protein wherein the cell expresses a GPCR or the protein is a GPCR.

113. (New) The compound of Claim Claim 64 wherein pharmacological properties are given as EC_{50} values for agonist stimulated – or pK_i values for antagonism of agonist stimulated second messenger generation.

114. (New) The compound of Claim 110 wherein spectral properties and fluorescent images are derived using the techniques of confocal microscopy or fluorescence correlation spectroscopy.